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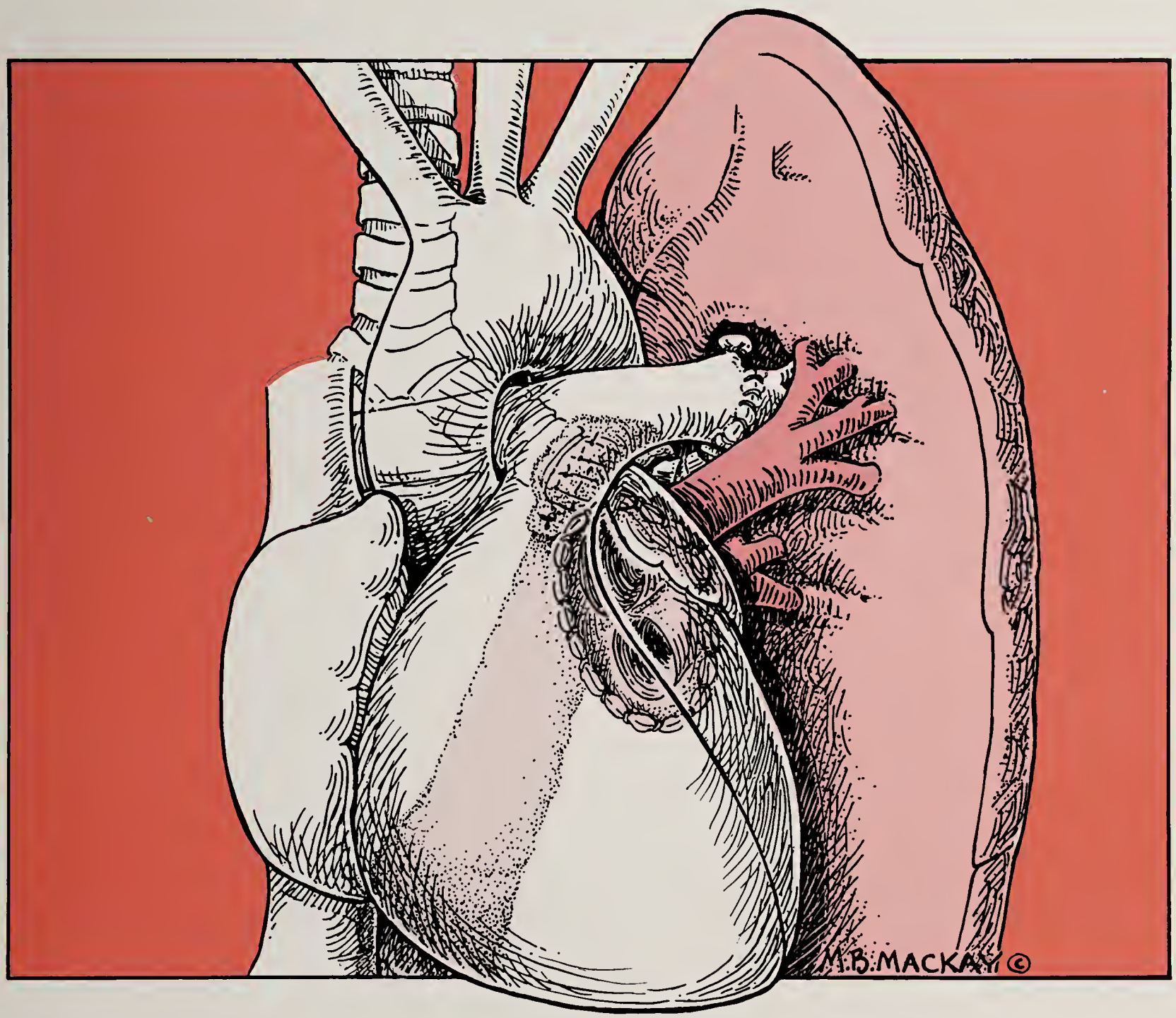

- Lung Transplant
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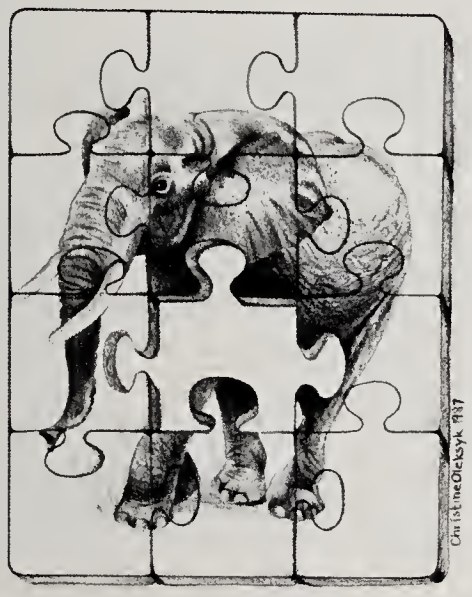
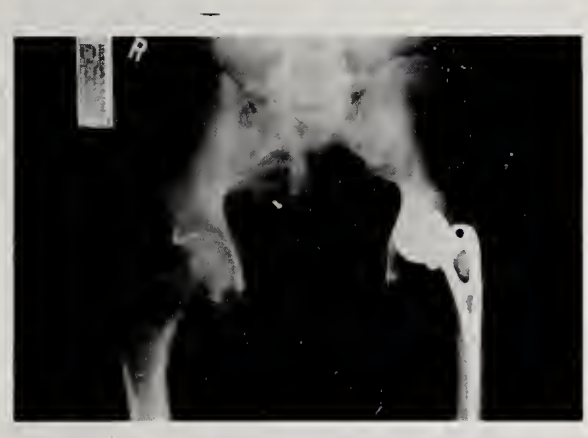
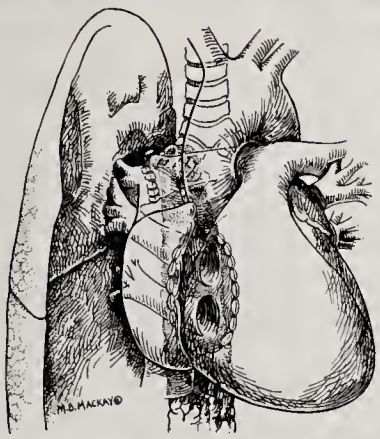


P. 4



P. 10



P. 14

P. 20

4 Immunology
IS ALZHEIMER'S DISEASE AN IMMUNE-MEDIATED DISORDER *(OR IS IT AN ELEPHANT)*?
by Sarah Borwein, M.Sc.

10 Orthopaedics
ALLOGENIC BONE TRANSPLANTATION IN RECONSTRUCTIVE SURGERY:
THE TORONTO EXPERIENCE
by Steve R. Mulholland, B.Sc. and Roger Oakeshott, M.D.

14 Thoracic Surgery
SINGLE LUNG TRANSPLANTATION AT THE UNIVERSITY OF TORONTO
by David Gluckman, M.D. and Joel D. Cooper, M.D.

20 Community Health
HEALTH SERVICES AND THE VENTILATOR DEPENDENT CHILD
by Stan Calderwood, M.D. and Raymond C. Tervo, M.D.

26 Human Sexuality
REFLECTIONS ON APHRODISIACS
by Shabir Bhimji and John R. Keller, M.Litt., B.Sc.

32 Respirology Rounds
SEVERE HEMOPTYSIS
by Folkert G. Zijlstra, M.D.,
Robert H. Hyland, M.D. F.R.C.P.(C),
Donald P. Jones, M.D. F.R.C.S.(C)
and Eugene L. St. Louis, M.D. F.R.C.P.(C)

35 Computers in Medicine

39 News Updates

40 Book Reviews

Cover Illustration:
Left lung transplant, showing the anastomosis of the left pulmonary artery, left atrial cuff anastomosis and the pedical of omentum wrapped around the left main bronchial anastomotic site.

Illustrated by Margot Mackay, Associate Professor, Department of Art as Applied to Medicine, Faculty of Medicine, University of Toronto.

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Editorial

Catherine Birt, Mike Paré and Raymond Ng
Editors-in-Chief

This issue is the first of the 65th volume of the *University of Toronto Medical Journal*. Our aim is to build on the tradition of our predecessors to achieve excellence in our student-run journal. To do this we have brought together a team of people, drawn from all four years of medical school and the art as applied to medicine program, who have worked hard and enthusiastically to produce this issue.

The major new section that we have added this year is *"News Updates"*. This is designed to acquaint our readers with ongoing research at the University, by giving brief descriptions of the work that is being undertaken by research scientists at the university and in the teaching hospitals. Another change that we have made is to have the position of Art Director filled by two undergraduates from the art as applied to medicine program, rather than by medical students, a move which seems to be both logical and practical. Finally, we have made a change to the list of the editorial board. Every member has chosen an area of special interest or expertise that they have, and will be providing a review of any submissions that we receive in that field (TCFOM stands for The Changing Face Of Medicine). We hope that this will further improve the quality of our reviews by giving articles to those most qualified to judge them.

The *U. of T. Medical Journal* has as variegated a readership as perhaps any other, and it is a challenge to produce an issue which will appeal to everyone. We are attempting to do so by publishing a wide range of topics, and choosing articles that are of interest to more than just specialists in that field. One of the ways we are attempting to encourage this is by offering, for the first time, an award for the best article published by the Journal. The winner, and two runners up, will be selected by the editors from among all the articles published this year, and the titles of their articles published in the third issue of the Journal. There will also be a cash prize of $100 for first place and $50 each for the two runners up. It remains to be seen how successful this innovation will be, but feedback from our readers is always appreciated and attended to. More than one prize winner will be published by the Journal this year, in fact. The department of Immunology sponsors an essay competition for second year students, and the winning article from last year, on Alzheimer's Disease, appears in this issue. The department of Orthopaedics also selects the winner of the R.I. Harris award from among the submissions in this field, which will be published later in the year. Finally, there is also a prize offered for the best article in the neurosciences - we hope that all these opportunities will stimulate students to write many good articles for the Journal!

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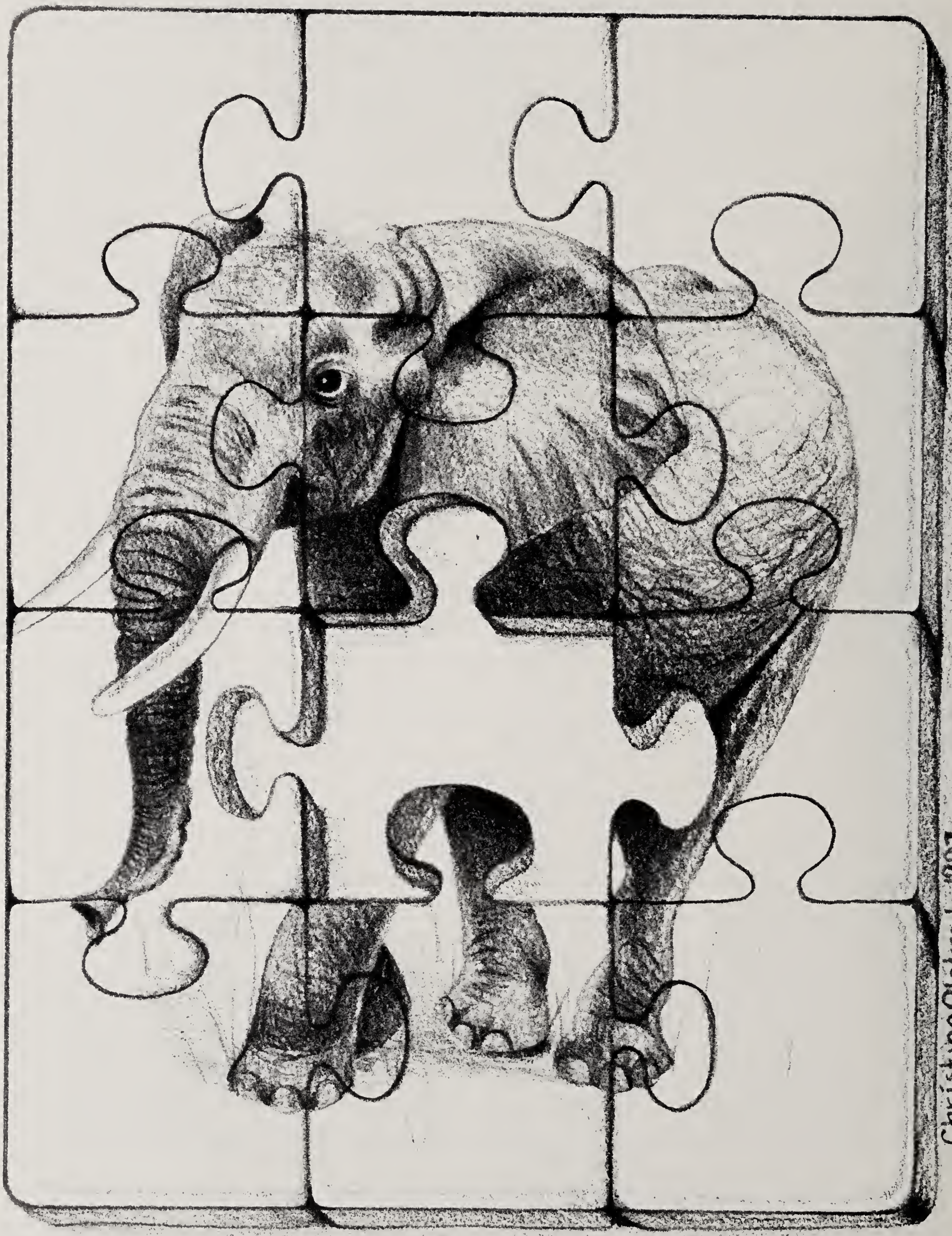

ChristineOleksyk 1987

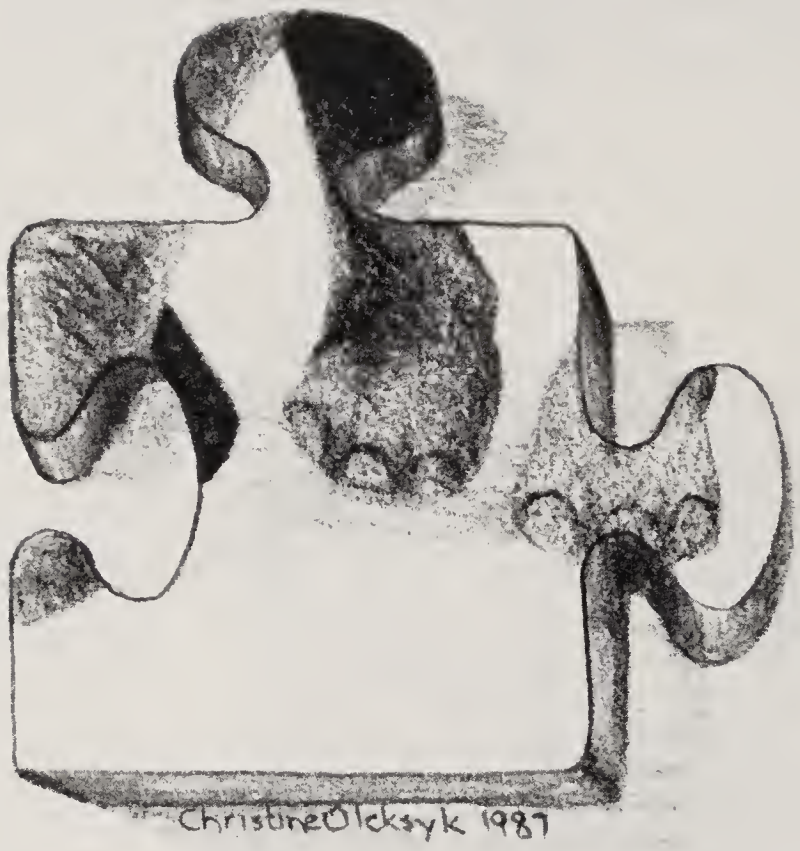
Is Alzheimer's Disease an Immune-Mediated Disorder?
(or is it an elephant?)

Sarah Borwein, M.Sc., 8T9

The six blind men concluded that an elephant was very much like a wall, spear, snake, tree, fan or rope - depending on the part they happened to touch. The elephant was all of these but they had not perceived its essential elephantness.

Eighty years after a German neurologist characterised the disease which now bears his name, Alzheimer's Disease (AD) remains a riddle wrapped in an enigma wrapped in a mystery. It is now the fourth leading cause of death in North America, and the major reason for institutionalization in nursing homes. And as life expectancy increases, the problem can be expected to grow. Yet, despite considerable efforts directed towards unravelling the mystery, the basic causes of the disorder remain elusive. Is it the result of a metabolic aberration, a genetic defect, a toxic accumulation or a failure of immunity? Is it an exaggeration of 'normal' cerebral aging or an independent disease whose susceptibility is increased by aging? This paper will examine the possibility that AD is immune-mediated, with emphasis on two major (and in fact related) theories: one, that the disease represents an autoimmune phenomenon; two, that it is caused by a slow viral infection.

Clinically, AD is a form of progressive dementia with increasing loss of memory, declining capacity for learning, failing judgement, disorientation for time, place and persons, and disintegration of personality. It usually occurs late in life (senile dementia) but is also recognized in early middle age (presenile dementia). Both the senile and presenile forms are now thought to represent the same disease and will henceforth be referred to as Alzheimer's Disease (AD). The histopathological lesions have been well documented. There is a loss of neurons, especially in regions essential for memory, cognition and thought, and in more primitive regions at the base of the brain which supply cholinergic innervation to cortical neurons. In the hippocampus and neocortex, there are numerous senile plaques, composed of amyloid, reactive cells and abnormal dystrophic neurons. Amyloid, aside from being found in senile plaques, is deposited in and around cerebral blood vessels. Neurofibrillary tangles consisting of paired hel-



ical filaments are also characteristic. Finally, granulovacuolar degeneration occurs in the cerebral cortical neurons. All of these lesions can be found in the normal aging brain, but their frequency is greatly increased in AD.

The notion that AD might be immune-mediated is tantalizing, if only because the immune and neuroendocrine systems are analagous in a number of interesting ways.[4] To begin with, each major class of immunocytes has an antigenic counterpart in CNS cells, but in no other cells. T-lymphocytes, for example, share certain antigens with brain cells and only with brain cells. In both systems, messages are transmitted between cells by soluble humoral factors; lymphokines and lymphotoxins fulfil this function in the immune system, neurotransmitters and neurotoxins in the CNS. Moreover, various immune cell subsets have receptors for endogenous neurotransmitters, and these receptors are identical to those found on brain cells. Finally, memory is a feature of both the immune and nervous systems but is found in no other system.

The significance of these similarities for understanding AD becomes more apparent when one adds to the above list the observation that both the immune system and the neuroendocrine system are subject to degeneration with aging. Since the incidence of AD increases as immune functions, particularly T-cell functions, deteriorate, one might speculate that the two trends are related. Changes in indices of immunological function would be expected in either altered brain autoimmunity or persistent viral infection of the brain. Both of these have been implicated in the pathogenesis of AD.

The Autoimmune Theory

Interest in the possibility that AD might be an autoimmune disorder was spurred by the finding that in AD brains both cerebral blood vessels and the core of senile plaques contain amyloid. Amyloid is a filamentous protein material commonly seen in chronic systemic inflammatory diseases, such as rheumatoid arthritis, which are thought to have an autoimmune component. In these diseases, vascular amyloid deposits may result from the processing of an abnormal serum protein by the lysosomal enzymes of endothelial cells. None, however, exhibit amyloid deposition in the brain. But if amyloid were to be produced in cerebral vessels, it could lead gradually to the breakdown of the blood-brain-barrier (BBB) and thus facilitate the entry into brain tissue of circulating elements (including virus!) that are normally kept segregated.

Recently, it has been shown that the amyloid of senile plaques contains complement components C1q, C3, and C4.[8] The fact that immunoglobulins, in particular IgG, are also present in the plaques suggests the existence of an antigen-antibody reaction or immune complex that activates subsequent complement binding. It is not known what kind of antigen(s) is introduced so massively in the AD brain, but it seems likely that some kind of immunological process - self-reactive or otherwise - underlies the deposition of amyloid fibrils.

Further evidence suggestive of autoimmunity comes from the demonstration by Nandy of brain reactive antibodies (BRAs) in the serum of AD patients.[11] BRAs are anti-brain autoantibodies which occur normally and naturally increase with aging, but which show a much greater increase in AD compared to age-matched controls. BRA formation seems to be related to thymic involution and age-related immunodysfunction and is thought to result from stimulation of the immune system by an autogenous rather than an exogenous antigen. Under ordinary circumstances, the BBB maintains separation between BRAs and brain tissue. As noted above, however, amyloid deposition could be associated with deterioration of the barrier, thus providing a portal of entry for the autoantibodies. At least in mice, intracerebrally injected BRAs are cytotoxic: antigen-antibody reaction and morphological damage are seen within days. Moreover, Nandy has bred a strain of mice which exhibit precocious BRA formation, and these mice behave as if 'senile' with respect to memory function. I would, however, add the caveats that the diagnosis of senility in mice seems suspect, and that in any case these mice do not show the specific neuropathological changes characteristic of AD.

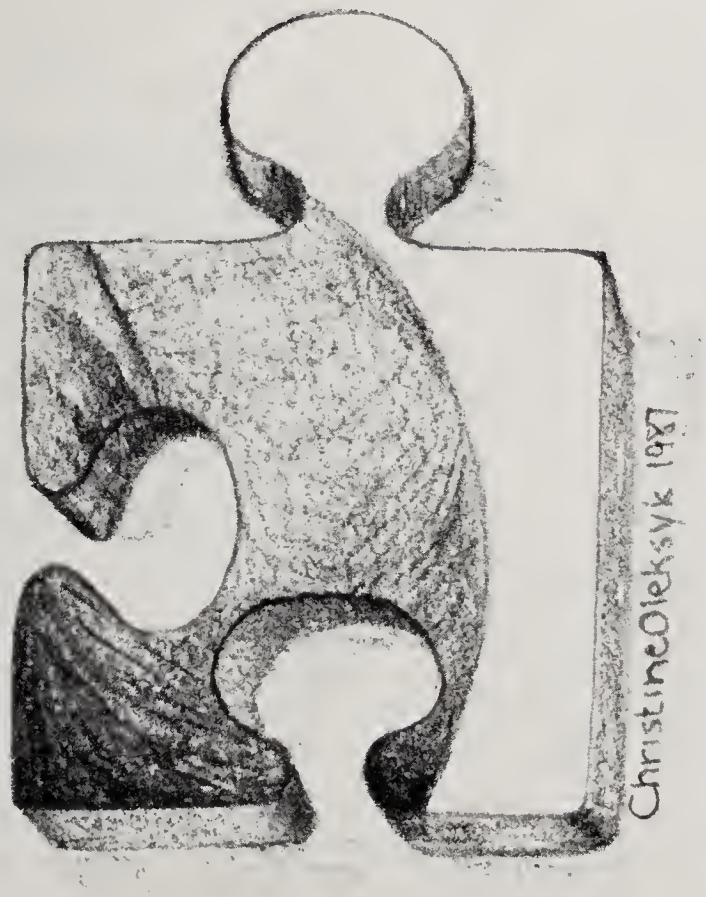
Finally, specific HLA genes are associated with a number of 'autoimmune' diseases, and there is some rather inconclusive evidence that there may be a correlation between HLA B7 and AD. Herbert reports that family studies involving 257 individuals, 51 of whom had AD, showed susceptibily carried on at least two genes on chromosomes 6 and 14.[7] Both of the genetic regions (HLA on chromosome 6 and immunoglobulins on chromosome 14) are involved in coding for normal immune function. While this is interesting and worthy of further investigation, it does not constitute proof or even good evidence that AD is an autoimmune disorder. Indeed, no significant abnormality has been found that indicates conclusively that AD has an autoimmune aetiology.

The Slow Virus Theory

If amyloid represents an immune complex reaction, where do the inducing antigens come from? One possibility is that they are related to a viral infection. Support for this notion comes from the existence of four dementias - kuru, Creutzfeld-Jacob Disease (CJD), scrapie and transmissible mink encephalopathy - in which a transmissible agent is known to be causative. Because the similarities between CJD, kuru (the two diseases from the above list which affect humans) and AD are stiking, both from a clinical and from a histological viewpoint, a number of researchers have suggested that AD may also have a viral or 'viroid' aetiology.[2,12]

Kuru, CJD and scrapie are caused by agents which are very small, have a long incubation period and are much more resistant to heat, formaldehyde and UV irradiation than are ordinary viruses. Prusiner has demonstrated that the agent responsible for scrapie is in fact not a virus but a small protein particle which he has termed a 'prion'.[12] Prions appear to be cytotoxic but not immunogenic, as no antibody production in the host is stimulated. To date no such particle has been isolated for AD but the search is on. There is, however, no evidence for an infectious aetiology in AD. No cellular reaction occurs in the CSF, no neutralizing antibodies have been found, immunity does not develop and, most importantly, there is no evidence of transmissibility. Still, although they are transmissible, kuru, CJD and scrapie also do not display inflammatory reactions in response to infection. The features shared between these diseases and AD, as well as the evidence that they may be caused by non-immunogenic prions, suggest that this line of research merits further attention.

Another interesting line of inquiry has arisen from the observation that Down's Syndrome (DS) patients consistently develop AD after the age of 40.[3] The brains of adults with DS possess granulovacuolar cytoplasmic changes, senile plaques and neurofibrillary tangles morphologically indistinguishable from and quantitatively similar to those in AD brains. The same areas of the brain are preferentially affected and there is an Alzheimer-like decrease in acetylcholine, cholinesterase transferase and norepinephrine. Now, Down's Syndrome, or Trisomy 21, involves a 50% increase in the dosage of genes found on chromosome 21. This has been directly demonstrated for four loci, one of which codes for the α-interferon receptor. The secondary effects of trisomy at this locus include a proportional increase in the synthesis of a series of interferon induced intracellular polypeptides and much enhanced sensitivity of trisomic cells to a variety of the actions of interferon. The actions of interferon include antiviral effects, an antiproliferative effect on fibroblasts, and an antimitogenic effect on lymphocytes. One could speculate that hypersensitivity to interferon might paradoxically affect immune function in an adverse manner and thus increase susceptibility to extrinsic or intrinsic infectious agents. In support of this speculation, it has long been known that DS individuals are highly susceptible to both bacterial and viral infections and that this is at least partly due to abnormalities of immune response. Specifically there is evidence of deficiencies and functional defects in T-lymphocytes.



The significance of these observations for understanding the pathogenesis of AD depends on how seriously one treats the possibility that AD is the result of an infectious process. It may be that AD and DS patients exhibit a similar immune dysfunction that predisposes both groups to a viral infection.

Miller et al. have shown that patients with AD show enhanced T-suppressor activity.[10] (It is not known whether there is a compensatory decline in the numbers of other T-cells). Interestingly, autoimmune diseases such as systemic lupus erythematosus, multiple sclerosis and acute graft-versus-host disease are characterized by **diminished** T-supressor activity. Elevated T-suppressor activity is a much rarer finding, but occasionally occurs in chronic graft-versus-host disease and a number of viral infections, in which suppressor cells probably cause immunological unresponsiveness. One might, therefore, postulate that AD represents a chronic viral infection in which there is enhanced immunological suppression. Alternatively, enhanced suppressor cell activity might result in impairment of a particular immune response and in this way allow an infectious agent to gain a foothold in the CNS.

In summary, evidence exists along several lines that Alzheimer's Disease has an autoimmune or slow viral component, or both. One can envisage a process whereby a slow viral infection leads to the formation of immune complexes. These may be catabolised by phagocytes and the immunoglobulin fragments degraded in lysosomes, resulting in extracellular amyloid deposition. Amyloid deposition in cerebral blood vessels would gradually wear down the BBB, allowing not only the virus, but also brain reactive autoantibodies, or perhaps exogenous toxins into brain tissue. More evidence is certainly needed before the precise role of the

immune system can be stated with confidence. It may well be that both autoimmunity and viral infection are involved, or that these processes are inseparable. It would be interesting to see if immunofluorescence labelling could track down the antigen(s) involved.

At this point, I should explain the subtitle of this paper and conclude by saying that, after all is said and done, I think that AD **is** an elephant. Because scientists, baffled, have tended to examine it in small pieces, many different explanations have been proposed for what this strange beast might be. Various investigators have suggested that AD is a genetic disease, an autoimmune phenomenon, a slow viral infection, the result of toxin accumulation, or the consequence of cerebrovascular degeneration. It is likely that it is all of these things, but in looking at the separate aspects of the disorder, science has failed to perceive its essential 'elephantness'.

I would propose that AD may well turn out to be a syndrome (i.e. an elephant) consisting of many facets and subtypes. Undoubtedly, some facets and perhaps even all subtypes of this syndrome involve immune dysfunction or the dissipation in the CNS of some immunocyte equivalent. But the immunology should be considered in symphony with genetics, biochemistry, toxicology (and so on) in order to understand the whole elephant.

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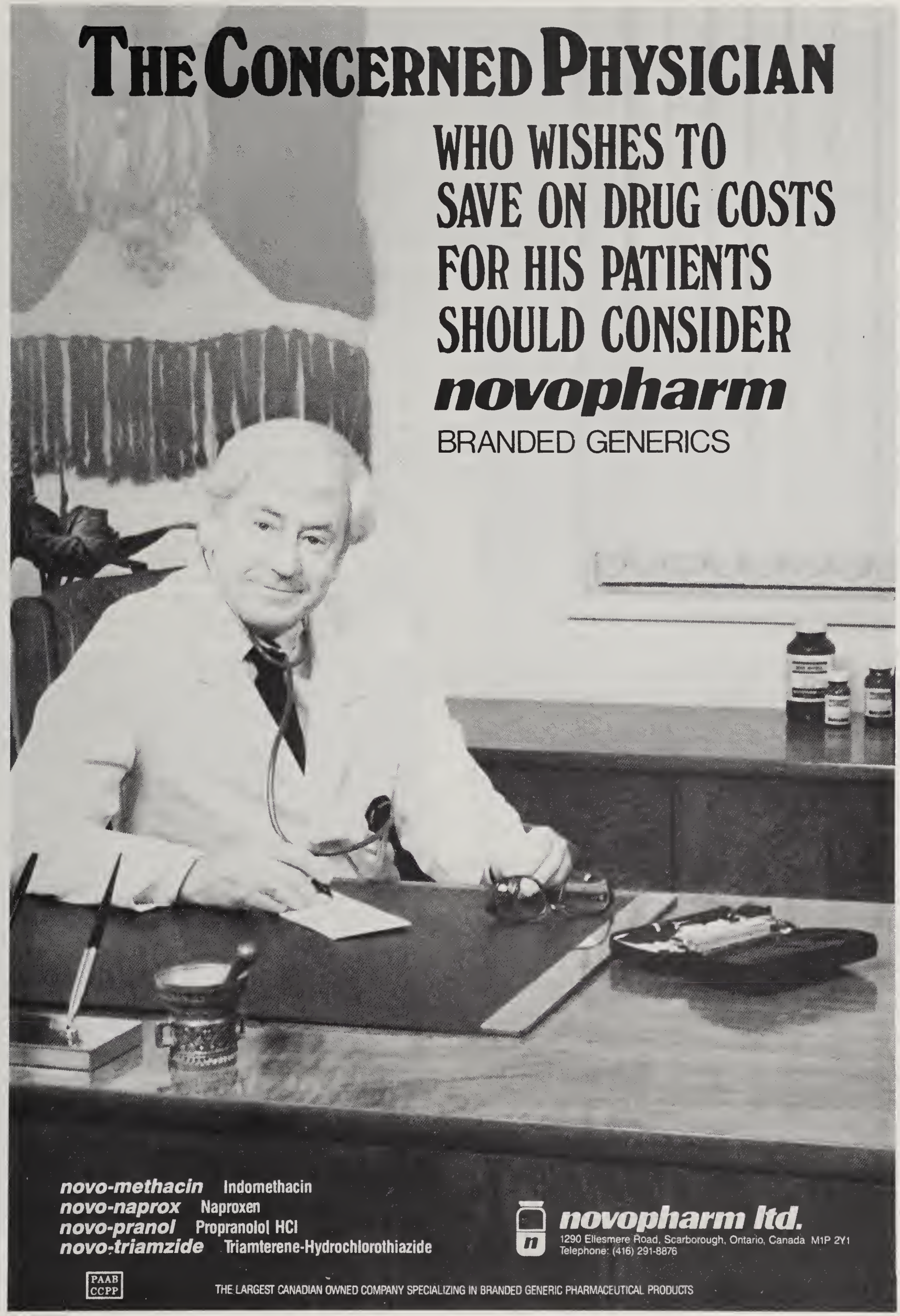

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Allogenic Bone Transplantation In Reconstructive Surgery: *The Toronto Experience*

*Steve R. Mulholland, B.Sc., 8T8 and Roger Oakeshott, M.D.**

Abstract

The University of Toronto has been at the very forefront of bone transplantation research and application since the formation of the Toronto Bone Bank in 1971. Over the past 15 years, the transplantation of allogenic bone has grown to become an important adjunct to the reconstructive surgeon. This paper summarizes the various roles of bone transplantation and presents 3 case reports to elucidate the applications of allogenic bone in reconstructive surgery.

Introduction

The transplantation of Bones and Joints is not a recent surgical procedure. Beginning with the pioneering work of Erich Lexer in 1908, scientific literature contains scattered reports of successful transplantation of both long bones and hemijoints.[6,10] However, because of early concerns over the biological compatibility of Bone Allografts (cadaveric bone transplanted from donor to recipient), and later, graft versus host reactions, many years elapsed before the practicality and clinical relevance of these surgical procedures became accepted.

During the last 15 years, transplantation of allogenic bone for the replacement of skeletal defects (and other osseous pathology) has gained widespread respectability. The early work of Parrish[14], Murray[12], Volkov[15], and Ottolenghi[13], demonstrated the effectiveness of allograft bone in the treatment of skeletal defects following bone tumor surgery. Recently, Gross[2,3,4] and Mankin[9], through innovation and concurrent clinical evaluation, have suceeded in expanding and more clearly defining the role of allogenic bone transplantation in reconstructive surgery.

The potential advantages of biological replacements when compared with metal and plastic implants has stimulated intense interest in bone transplantation. Allografts (allogenic bone transplants), for example, may be individually tailored during a surgical procedure. Tendons and ligaments may be preserved with the allograft to provide a more anatomical and physiological result. Some longterm studies have reported excellent results following the transplantation of fresh, small fragment ostoechondral allografts (segments of bone which are transplanted along with their articular cartilage).[11] With creeping boney substitution and revascularization of the allograft by the host, biological fixation by boney union becomes ensured. This biological union alleviates the problem of boney resorption at the metal to bone interface as is seen with other implants.[11] Chondrocyte viability in these fresh, small osteochondral allografts is excellent. Malin *et al*, has employed various cellular studies which indicate that in those allograft bone specimens which have been cryopreserved prior to transplantation, some chondrocyte function remains.[8,9] This chondrocyte viability, therefore, allows for true biological joint resurfacing. Sterility of these grafts is not a problem. With 2.5 megarads of irradiation, the frozen grafts can be rendered completely bacteria and virus free, while the fresh grafts are biopsied and cultured to ensure bacterial contamination does not occur.[5] In addition, the boney component of the graft may be irrigated with a 0.3% hydrogen peroxide solution to prevent transmission of HIV and other viral or viroid like organisms.[5]

The Toronto allograft bone transplantation program was conceived in 1971. Since that time the role of allograft transplantation in reconstructive surgery has been expanded. It now includes:

1) Fresh, Small Fragment Osteochondral Allografts (a small segment of donor bone which also contains articular cartilage).
2) Larger, Intercalary/Segmental Allografts (donor bone which is used to span defects).
3) Large Osteoarticular Allografts (a large piece of donor bone which also includes articulated cartilage). (Table 1)

The following case histories illustrate the most common applications of allogenic bone transplantation in reconstructive surgery.

* *Clinical Fellow, Combined Toronto General Hospital/Mount Sinai Hospital Orthopaedic Services*

Table 1. Bone Allograft Classification for the University of Toronto Comprehensive Transplant Program.

Size	Type	Storage	Transplantation Role
Small Fragment	Osteochondral	Fresh	Trauma
		Frozen	
Large Fragment	Osteoarticular	Fresh or Frozen	Tumor
	Segemental		Arthroplasty
	Intercalary		Trauma

Case Reports

Case 1 TRAUMA: Fresh, Small Fragment Osteochondral Allografts

This case involves a 46 year old male logger, who sustained a left lateral tibial plateau fracture when his left knee was struck by a tree, in July of 1984. Primary treatment at that time consisted of an attempted open reduction and internal fixation of the fracture (Fig. 1). Due to technical problems with the procedure and a significant crush component to the fracture, the patient was left with an unstable left knee, with substantial loss of bone and articular cartilage on the lateral tibial plateau, resulting in a progressive valgus deformity. The patient experienced episodes of "giving way", physical examination revealed him to have a range of flexion from 10 to 90, with an obvious genu valgum. His functional status was such that he was confined to a walker or crutches and was unable to gain full time employment.

Figure 1: Case 1 This x-ray reveals attempted internal fixation of the left lateral tibial plateau fracture. The bone and articular cartilage loss is evident. The left knee is in a significant degree of valgus.

A fresh, small fragment osteochondral allograft was transplanted into the left lateral tibial plateau on October 29, 1985. Concomittantly, a distal femoral varus osteotomy was performed to decompress the lateral compartment of the knee (Fig. 2).

Figure 2: Case 1 This x-ray reveals the Fresh, Small Fragment Osteochondral Allograft in situ. Internal fixation has been employed to stabilize the graft and a AO plate has been used for compression of the Distal Femoral Varus Osteotomy. Osteotomy is performed to decompress the lateral compartment and thus protect the allograft by producing a vaurs angulation at the knee.

Currently, 21 months following bone transplantation, the patient is pain free, has a full ROM (0°/120°), and is experiencing no instability. He should return to full time employment in 3 months, after being weaned off his brace.

Case 2 ARTHROPLASTY REVISION: Large Fragment, Intercalary Allograft

This case involves a 26 year old man, who suffered an intracapsular fracture of his left hip. This occured in 1975, when the patient was 18 years of age. Primary treatment at that time involved the insertion of an Austin Moore hemiarthroplasty. However, due to increasing pain in the hip, the patient became severely disabled and was unable to continue on in his occupation as a janitor.

9 years following the accident, he presented with an antalgic gait, a limited range of hip motion, and a leg length discrepancy of 3 cm. X-rays revealed significant superior and medial protrusio acetabulare (medial migration of the acetabular component), (Fig. 3). In addition, the film showed a lucent line around the stem of the Moore hemiarthroplasty, indicating evidence of loosening of the implant.

Due to the high physical demands on the patient, an arthrodesis (fusion) was deemed the most appropriate form of surgical intervention. Fusion was accomplished by the use of a large, intercalary allograft which was

Figure 3: Case 2 This x-ray of the pelvis illustrates an Austin Moore Hemiarthroplasty of the left hip, at 9 years postoperatively. The Austin Moore prosthesis has caused superior and medial protrusio acetabulare. A lucent line is evident on the medial aspect of the Moore arthroplasty, indicating loosening of the prosthesis in the femoral shaft.

Figure 4: Case 2 This x-ray of the pelvis, taken 20 months postopertively, illustrates the Large Fragment, Intercalary Allograft, with internal fixation employed to fuse the left hip joint.

fashioned to replace the area of the severe bone loss in the acetabular region (Fig. 4).

20 months following surgery, the left hip is clinically and radiologically fused and the patient has returned to full time employment.

Case 3 TUMOR: Large Fragment, Osteoarticular Allograft

Figure 5 is a x-ray illustrating an osteosarcoma in the left humerus of a 14 year old male. The patient had a 7 month history of pain over the lateral aspect of his left arm and had suffered a weight loss of 20 lbs. Following confirmatory biopsy, the patient underwent preoperative, adjuvent chemotherapy.

As a full metastatic series of investigations failed to demonstrate any evidence of tumor spread, the patient was deemed suitable for limb salvage procedure. On August 5, 1986, an en bloc excision of the left humerus was performed, with a total humeral allograft replacement. While the surgery involved resection of the deltoid, long head of biceps, brachialis, and the insertions of the rotator cuff muscles, the brachial plexus remained intact, apart from the circumflex nerve. The patient was discharged from hospital on the 5th postoperative day.

Review at 8 weeks post-operatively revealed full hand function with no loss of sensation, decreased elbow ROM, and a limited range of motion of the shoulder. His x-rays are as illustrated in Figure 6.

Figure 5

Figure 6

Figure 5: Case 3 This x-ray is of an osteosarcoma in the left humerus in a 14 year old male. The extensive subperiosteal new bone formation can be seen extending from the region of the epiphysis of the humeral head to the mid-diaphyseal region of the humerus. Areas of sclerosis within the humerus reveal the osteogenic nature of the tumor.

Figure 6: Case 3 This is an x-ray of a total humeral allograft resection of the humerus. Weck clips can be seen along the line of the cephalic vein and its tributaries.

Discussion

Allograft bone transplantation has a wide range of applications in reconstructive surgery. These include the replacement of bone and/or cartilage defects as is seen in trauma, tumor, revision total joint arthroplasties, and congenital defects.

Allograft transplantation allows for limb salvage procedures in patients who would have previously, almost invariably, undergone amputations. Allografting also provides the ability to retain motion in a joint which previously, due to excessive damage to the articular cartilage, would have been suitable only for an arthrodesis. In the area of total joint arthroplasty, allograft bone transplantation has provided the ability to repeatedly revise hips and knees, where previously patients would have been destined for a bed to chair, or

wheelchair, existence. This revision of total joint arthroplasties constitutes approximately seventy percent of allograft procedures in Toronto.

Unlike other forms of transplant surgery, bone and cartilage allografting does not require immunosuppressive treatments.[5] The immunogenicity of bone and cartilage is minimal and is perhaps reflected mainly by delays in union of the graft to the host, when compared to ordinary fracture healing.[5] There are no viable cellular components in the osseous portions of the grafts, and the cellular components of the cartilage are held within matrix and are therefore protected from immunological reactions.[5,11]

With regard to the fresh, small and large fragment allografts, intensive laboratory investigations prior to the transplantation ensure maximal precautions are taken to prevent the transmission of disease. In addition, all frozen grafts receive a 2.5 megarad irradiation conferring complete sterility.[1]

While these transplants are not without their complications, including infection, fracture, resorption, compression, and fragmentation, their results are sufficiently good to provide an acceptable, biological alternative to, (or in combination with) metal and polyethylene prostheses. Current research and experimentation includes meniscal and ligamentous transplantation in combination with the osteochondral elements previously described. Research on synthetic bone substitutes continues, but, at present, allogenic bone transplantation has shown clinically superior results.

Thus, the growing number of Bone Banking centers in community hospitals is a reflection of the important role of bone transplantation in reconstructive surgery.

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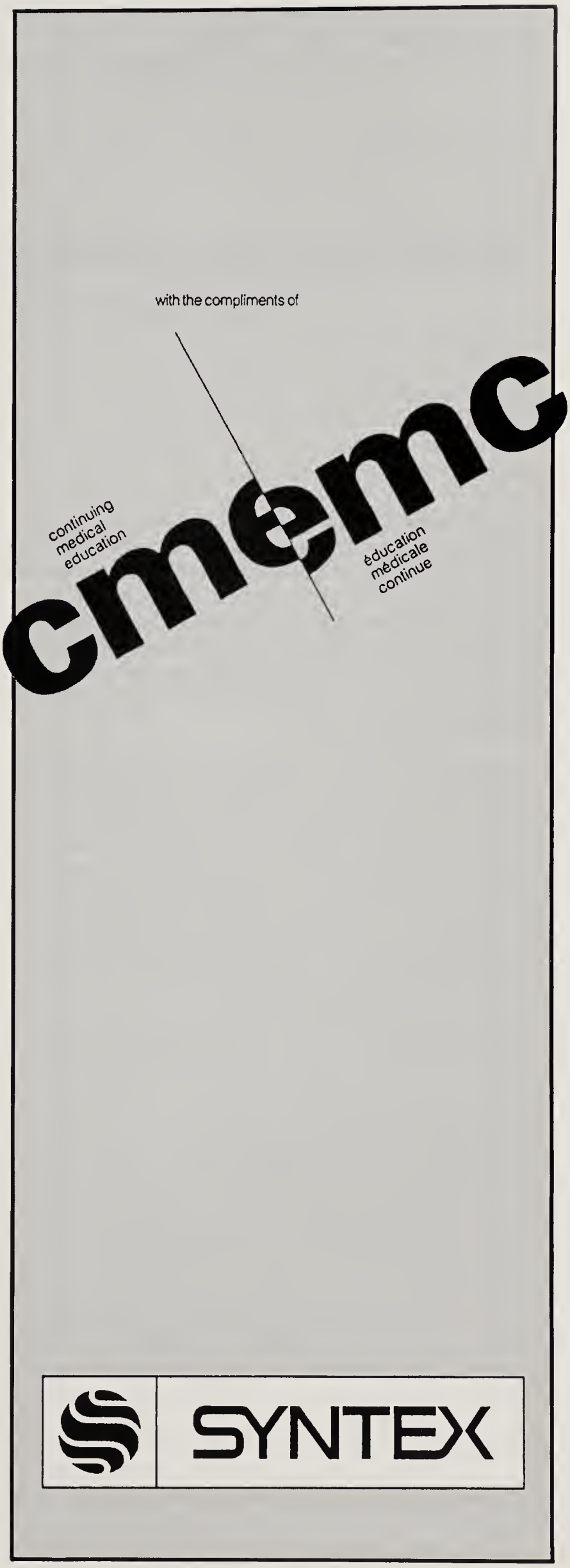


Single Lung Transplantation at the University of Toronto

David Gluckman, M.D. and Joel D. Cooper, M.D.

Successful single-lung transplantation has been accomplished at the University of Toronto following a lengthy period of poor worldwide results. There are ning long-term survivors of eleven single lung transplants that range in post-operative survival from 5 months to 44 months (mean 15.8 months, median 7 months). These patients have had excellent functional results. The recent success had resulted from several years of clinical and laboratory investigation that has demonstrated improved bronchial healing resulting from the use of cyclosporine and azathioprine immunosuppression, bronchial omentopexy, and the avoidance of routine steroid administration in the early post-operative period. These technical aspects of success were achieved in a setting of improved patient selection, efficient donor procurement, and the efforts of a well co-ordinated team of medical, nursing, and rehabilitation specialists.

Successful clinical transplantation for end-stage respiratory disease has now been accomplished at the University of Toronto following a lengthy period of poor worldwide results. The recent success has resulted from several years of both clinical and laboratory investigation under the direction of Dr. J.D. Cooper, Head of the Division of Thoracic Surgery at the Toronto General Hospital. These efforts have produced the world's nine patients having long-term survival following single lung transplantation.

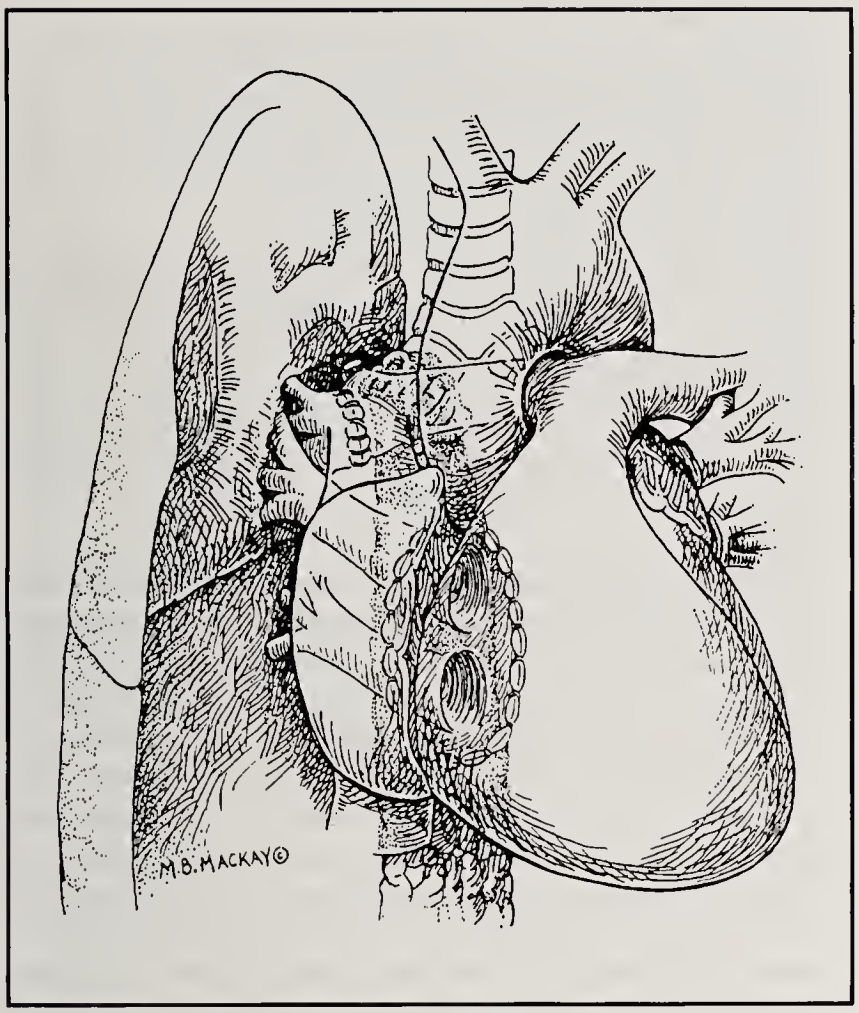
Between 1963 and 1980, there were 38 attempts in various centers at single lung transplantation with very limited clinical success. Approximately 29 patients succumbed within 2 weeks, most often to respiratory failure secondary to rejection, infection or other causes. Of the 9 patients surviving longer than two weeks, approximately 6 died in the third week from complications of the bronchial anastomosis. Of the three remaining patients, the longest survivor lived for ten months and was the only recipient to leave hospital, albeit for only a two week period.[1,2]

The first single lung transplant at the University of Toronto was done in 1978 at the Toronto General Hospital in a 19 year old male who had experienced respiratory burns and had remained ventilator-dependent for 6 months.[3] With the assistance of pre-, intra- and post-operative extracorporeal membrane oxygenator support (ECMO) the transplanted right lung functioned well. After several days all ventilatory support was discontinued. He died, however, in the third week of bronchial disruption.

Following the absence of clinical success, and a 25% incidence of bronchial complications, including stenosis, dehiscence, necrosis with aspiration, bleeding, peribronchial abscess, and pulmonary artery-bronchial fistula, further human lung transplantation in this institution was halted. Laboratory research using dogs was then undertaken to investigate the cause of impaired bronchial healing.

As with any major organ transplant, the healing process may be adversely affected by rejection, infection, drug therapy, and the general debility of the patient. In lung transplantation an additional problem is ischemia of the donor bronchus which has been completely severed from its systemic blood supply and is dependent on collateral blood flow from the pulmonary circulation which has a low pressure and low O_2 content. The period of ischemia persists for approximately 12-15 days post-operatively when adequate revascularization from the recipient bronchus is established.[4,5]

Several unsatisfactory methods of improving bronchial healing have been reported including wrapping the anastomosis with perihilar connective tissue,[6] telescoping the bronchial ends,[7] and shortening the length of the donor bronchus.[8] Microsurgical techniques have been employed to reanastomose the bronchial arteries with consequent improvement of bronchial healing.[9,10,11] As an easier, more reliable alternative, a pedicle of omentum was passed sub-sternally and wrapped around the bronchial anastomosis. The omentum possesses a rich vascular and lymphatic supply and has been used in various situations to establish new vascular and lymphatic communications and to promote repair in areas of poor healing such as treating



established broncho-pleural fistulas and bronchial stumps.[12,13,14,15,16,17]

Using omental pedicle wraps, the bronchial anastomosis in canine lung transplants and in canine bronchial transplants was studied in the laboratory.[18,19,20] The chest x-ray, gross and microscopic appearance of the anastomosis, cross-sectional area of the anastomosis, and vascular studies with injected radiopaque microfil were performed. Although bronchial complications are less common in canine than human lung transplants, the bronchi without omental wraps showed varying degrees of mucosal ulceration, necrosis, granulation tissue, separation or stenosis, while those with omental wraps showed a normal bronchial architecture with revascularization as early as 4 days. The results showed that the omental pedicle wrap could be of value in bronchial healing in human lung transplantation.

High dose azathioprine and corticosteroids have been traditionally employed for immunosuppression. However, the lung is unique as an organ graft in that it is continuously exposed to airborne organisms from the environment and possibly from the contralateral lung. Corticosteroids render the recipient prone to infection and have been proven to significantly retard bronchial healing.[21] Cyclosporine, however, has been shown to be an effective immunosuppressant in various animal models and in humans, acting mainly against T-lymphocytes.[22,23,24] It has also been shown to have little effect on tissue healing, to spare polymorphonuclear leukocytes, and to be more effective than conventional immunosuppression in prolonging survival and reducing morbidity in the canine lung allotransplant model.[23,25,26] Hence, cyclosporine was assessed in the laboratory for its immunosuppression in canine lung allotransplantation and in combination with an omental pedicle wrap for its ability to prevent bronchial complications particularly late bronchial stenosis.[27]

The laboratory studies demonstrated that cyclosporine and azathioprine immunosuppression, and bronchial omentopexy were a good combination for minimizing bronchial complications that are a frequent cause of death in human lung transplants. Based on these results and continued experience with an extracorporeal membrane oxygenator as a support for respiratory failure that could be used to support lung transplant patients as needed in the pre-, intra-, or post-operative phase, an experimental program in human lung transplantation was resumed.

The first patient was a 31 year old man suffering from progressive respiratory failure secondary to prolonged paraquat poisoning.[28] On transfer to TGH from Atlanta, Georgia on August 24, 1982 he had been on ventilator support for 10 days, had pulmonary sepsis and paralytic ileus, and was in renal failure. Despite charcoal hemoperfusion, high dose steroid therapy, multiple antibiotics, and bleomycin in an attempt to prevent the inevitable pulmonary fibrosis associated with paraquat poisoning, his condition deteriorated and he soon required ECMO support. A right lung transplant was performed on August 29, 1982 using cyclosporine and azathioprine for immunosuppression and an omental wrap, with ECMO support intraoperatively and continuing for 24 hours post-operatively. Despite continued hemodialysis and charcoal hemoperfusion post-operatively, high muscle stores of paraquat caused blood paraquat levels to rise dramatically. The transplanted lung was seriously injured and he subsequently went into respiratory failure requiring 17 days of additional ECMO support with charcoal hemodialysis to reduce the paraquat levels. A left lung transplant was then performed employing a pericardial wrap around the bronchus, as the omentum was no longer available. Blood gas exchange remained adequate for the next ten weeks until the patient's death. However, he developed several lung infections, and never recovered from the paraquat-induced renal failure and a progressive toxic myopathy that left him ventilator-dependent. Despite his many complications, the patient remained alert, and comfortable, and actively participated in his rehabilitation program. Ten weeks after the initial transplant he died from a tracheoinnominate artery fistula and subsequent stroke. Autopsy showed no histologic evidence of rejection, a well-healed left bronchial anastomosis, and a narrowed but firm right bronchial anastomosis, and healing of all surgical wounds by primary intention.

This case yielded useful information. It showed that ECMO could be used to provide support for extended periods of time to the recipient in respiratory failure prior to finding a donor, intra-operatively, or in the patient suffering from early post-operative respiratory failure or rejection. It also showed that the bronchial anastamosis complications and rejection can be effectively managed using the techniques of omental wrap, and cyclosporine plus azathioprine for immunosuppression.

In reviewing this case and the previous history of lung transplant attempts it became evident that the criteria for patient selection were inadequate. Most

transplantation was done as a life-saving attempt in these people who were debilitated, often had respiratory sepsis, and lacked the strength to breathe on their own following transplantation. Lung transplant candidates in this center have now been restricted to patients with progressively deteriorating end-stage chronic pulmonary disease that is refractory to all known alternate therapies. These patients require continuous oxygen, and have a predicted life expectancy of approximately 6 months to 1 year. Each patient has to be highly motivated towards obtaining a transplant, and aware of the previous failures of the procedure. Patients ideally suited are those with pulmonary fibrosis. Contraindications to single lung transplantation include patients who are dependent on a ventilator, those who cannot be weaned from chronic steroid therapy, and patients with emphysema, bilateral pulmonary sepsis, or patients with end-stage right heart failure. Prior to transplantation, each patient is reviewed and approved by an independent ethics committee comprised of three physicians.[29]

A major obstacle to lung transplantation is the scarcity of donors. Suitable donor lungs are extremely rare, and of those donors now available for other organ transplants, not more than 1 in 10 have lungs suitable for lung or heart-lung transplant. Pulmonary edema, infection, or contusion is frequently present when an individual becomes available as donor. In the case of the paraquat victim it was necessary to accept a donor with a proven lung infection after waiting for 8 days with the patient on ECMO. For the donation of a lung, the individual must have a clear chest x-ray, and nearly normal pulmonary gas exchange. The size of the donor lungs must match the size of the recipient's chest. These prerequisites are rarely present, and reduce the number of potential donors. Progress has been also limited by the absence of reliable methods of lung preservation so that harvesting and transplantation must occur in the same institution rather than geographically separate ones.[33] Recently however, lungs were successfully utilized that were removed at another center and then transported to the Toronto General Hospital. The excised lung is immersed in 4°C Collin's solution and post-transplant function has been excellent with ischemic times of up to 4 hours.

The limited success under difficult circumstances achieved in the paraquat victim, and the clinical success reported with combined heart-lung transplant[30] encouraged further lung transplantation. The clinical course of the two subsequent single lung transplantation patients is outlined in the following case histories.

Case 1

A 58 year old male presented in September 1981 with cough, fatigue and a three year history of progressive exertional dyspnea, and was diagnosed as having idiopathic pulmonary fibrosis. By November 1982, despite increasing doses of corticosteroids, he had deteriorated, having hypoxemia at rest and desaturating with minimal activity. Supplemental nocturnal oxygen was begun and he was started on a four month course of D-penicillamine. He experienced an acute exacerbation of his pulmonary disease in February 1983 which was treated with oxygen, steroids, and antibiotics. From this point onward he became completely oxygen-dependent. By June 1983 there was clinical, radiological, and physiological evidence of progressive deterioration with respiratory failure despite aggressive medical management. The patient was accepted for lung transplantation, and in November 1983 he received a transplanted size-matched healthy right lung. Immunosuppression was maintained using azathioprine and cyclosporine. He was extubated on day 3, but required subsequent mechanical ventilation, and boluses of corticosteroids and antilymphocyte globulin for acute episodes of rejection on day 6 for 48 hours and on day 16 for 48 hours. Daily prednisone was instituted at 21 days. He was permanently removed from supplemental oxygen at three weeks maintaining a resting pO_2 of 80 mmHg, and bronchoscopy showed adequate bronchial healing. Although he showed no O_2 desaturation with exercise, his exercise tolerance was poor for approximately 4 weeks following transplant. He was discharged from TGH at 6 weeks to a chest rehabilitation center, and subsequently demonstrated progressive improvement in exercise tolerance. Immunosuppression was maintained with cyclosporine and prednisone and he has had no subsequent episodes of rejection. He resumed his previous work 3 months post-operatively and continues to lead an essentially normal life with slight dyspnea when climbing hills or stairs.

The initial poor exercise tolerance in spite of adequate blood gas exchange following surgery was felt to result from muscle fatigue rather than oxygen desaturation. His inactivity because of longstanding oxygen-dependency had led to severe muscular deterioration which was improved post-operatively by the rehabilitation program. As a result a pre-operative physical rehabilitation program for all transplant candidates was instituted. Subsequent transplant recipients have demonstrated a more accelerated recovery.

Case 2

A 35 year old female presented in February 1977 with a three month history of progressive exertional dyspnea, mild cough, anorexia, and weight loss. No therapy was instituted until July 1979 when she was re-assessed and found to have markedly decreased exercise tolerance and clinical evidence of pulmonary hypertension. Following a diagnosis of idiopathic pulmonary fibrosis she was treated unsuccessfully with several courses of oral corticosteroids. Upon reassessment in June 1982, she was demonstrated to have mild pulmonary hypertension which worsened dramatically with exercise. Mild hypoxemia was present at rest but marked arterial oxygen desaturation occurred with minimal exercise. She was discharged on continuous oxygen therapy. By October 1984, she had deteriorated clinically, radiologically, and functionally. She was demonstrated to have CO_2 retention and progressive pulmonary hypertension, maintaining mobility only by means of an electric wheelchair. The patient was accepted for lung transplantation and, following a 5 week wait, an oversized left lung was transplanted on November 30, 1984, with the belief that she might not survive long enough for another donor to be found. Her immediate post-operative ventilatory and hemodynamic status was stable. An early episode of rejection was successfully managed with cyclosporine and antilymphocyte globulin, and she was extubated on day 9. However on day 10 she was reintubated for an episode of severe rejection. She was again extubated on day 15, requiring no further ventilatory assistance. By day 20 the patient was up walking with supplemental oxygen, and by day 45 she was discharged to a rehabilitation unit where she underwent a progressive exercise program involving calisthenics and bicycle ergometry. At the end of a two week training period she was fully ambulatory, independent, and had a fair exercise tolerance. Her resting arterial blood gases were normal, and she did not significantly desaturate with exercise. Her vital capacity has doubled from preoperative values. Presently the patient is living a normal life, works regularly, and is unaware of any restriction. Pre-operative and post-operative chest x-rays are demonstrated in Figure 1.

Nine additional lung transplantations have been performed to date, with seven post-operative survivors. Further details concerning these patients are listed in Table 1. The success in these cases can be attributed predominantly to improved bronchial healing resulting from the use of cyclosporine, the use of an omental wrap, the avoidance of routine steroid administration in the early post-operative period, and to improved patient selection. These technical aspects of success could only be achieved, however, with a well co-ordinated team of people with diverse areas of expertise including respirology, anaesthesia, intensive care, high quality nursing, nutritionists, respiratory and physical rehabilitation, psychological assessment and support, and efficient donor procurement.

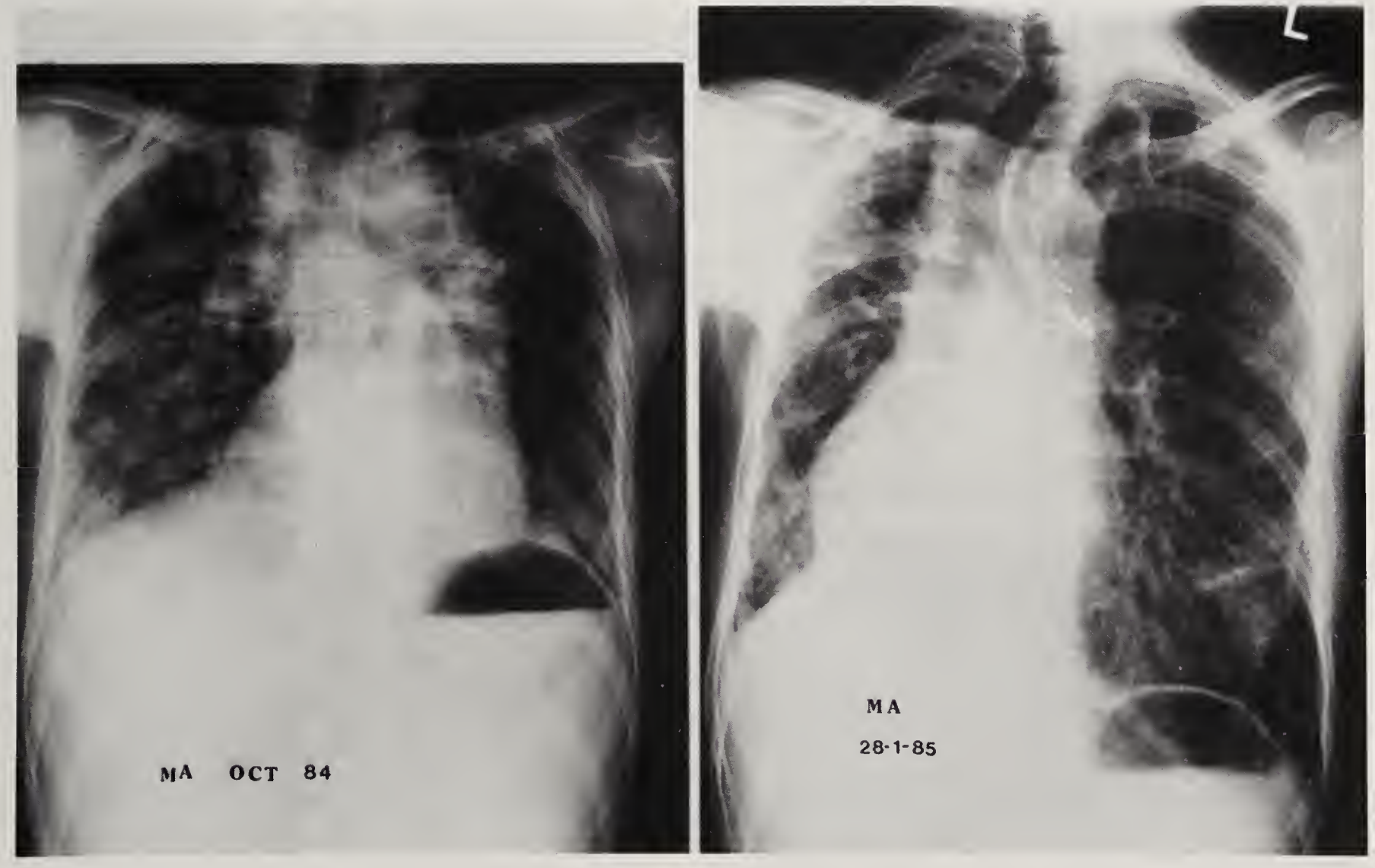


Figure 1. Chest X-rays of Patient 2, taken before and after transplantation.
The film taken 2 months after left-lung transplantation shows marked expansion of the left chest and a shift of the mediastinum because of insertion of an oversized left lung. Note the normal configuration of the left hemidiaphragm despite its downward shift.

Currently, clinical and laboratory research is being extended by the thoracic division to include other areas of transplantation for respiratory disease. For patients with chronic respiratory disease and secondary cardiac failure, a clinical and laboratory program has been developed for combined heart and lung transplantation. This is referred to as a lung-heart transplant to emphasize its application to patients with pulmonary disease. A new procedure for combined en bloc double lung transplantation has been developed for those patients requiring a double lung but not a heart transplant. Other laboratory investigations in the area of transplantation for respiratory disease include studying methods of lung preservation, biochemical markers of rejection, and developing a model of chronic pulmonary hypertension and right ventricular failure to determine the degree of recovery of ventricular function after the restoration of normal pulmonary vascular resistance.

Table 1:
Results of Single Lung Transplantation

Patient	Age	Sex	Cause of Pulmonary Fibrosis	Side of Transplant	Survival	Current Status
1	58	M	Idiopathic	R	44 mos	s
2	35	F	Idiopathic	L	31 mos	s
3	51	M	Idiopathic	L	POD	d
4	45	M	Idiopathic	R	20 mos	s
5	56	M	Idiopathic	L	17 mos	s
6	56	M	Idiopathic	L	7 mos	d
7	59	M	Idiopathic	L	POD	d
8	15	M	Familial	L	6 mos	s(1)
9	48	M	Idiopathic	L	6 mos	s
10	49	M	Idiopathic	L	6 mos	s
11	44	M	Sarcoidosis	L	5 mos	s

R = right
L = left
POD = post-operative death
s = alive and well
d = deceased
(1) = alive with lymphoma

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Health Services and the Ventilator Dependent Child

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Abstract

More children are surviving spinal cord injuries that leave them quadraplegic and dependent on respirators. This requires continuous medical care which traditionally has been supplied in the hospital setting of an Intensive Care Unit. This article discusses the advantages and requirements of instituting a home care system for these children.

More spinal cord injured pediatric patients are surviving because of recent developments in health care. These developments include improvements in respiratory support and maintenance technology and in the delivery of acute care, including the introduction of regional trauma units (ICU), neonatal (NICU) and pediatric intensive care units (PICU)[1, 2]. Mortality associated with spinal cord injury, which was as high as 12 times that of an age matched normal population in 1961,[3] is decreasing so that the life expectancy of survivors is increasing. Most cervical cord injuries occur in young people less than 24 years of age.[4]

Cervical cord injuries frequently leave the patient quadraplegic and requiring respiratory assistance. Therefore, improved health care has led to an epidemic number of young people requiring long term life support measures. Currently many of the cervical cord injured patients spend long periods in acute care settings because of the scarcity of appropriate long term facilities.[8] Keeping these patients in acute care settings is expensive in both human and economic terms, highlighting the need for a well co-ordinated regional program for the long term care and rehabilitation of the ventilator dependent pediatric patient.

This article develops the concept that home care may be a sensible alternative to hospital care for the young respirator dependent quadraplegic and discusses an approach to development of a home care program.

The Need For Change

The acute care hospital and especially the modern ICU is a poor environment for rehabilitation.[4, 12] The acute care setting emphasizes care delivery. The patient is a recipient of care and the medical and nursing staff are the providers of care. This approach, essential for treatment of the acutely ill patient, is counter to the desired approach for the chronically disabled patient where management focuses on enhancing function. Rehabilitation is a process of learning to cope with one's own disability in one's own environment which transfers the responsibility for patient care, wherever possible, to the patient. In the acute care setting the patient is isolated from the challenges of daily living and is provided with little opportunity or incentive to develop the skills necessary to cope with his condition. The patient is also isolated from family and friends and is surrounded by sick people. This has a negative influence on social and spiritual well-being which is of prime importance in encouraging independence. If the spinal cord injured patient is to be rehabilitated, an alternative to the acute care hospital must be found.

The acute care setting can be very disruptive to a child and family for a number of reasons. The parents are used to being the prime care givers in the rearing of the child. When the child is kept in the hospital, the parents too frequently find they have lost control. They must drive long distances to see the child; they must abide by a hospital schedule which often results in long waits, time off work and decreased independence. They are left out of decisions concerning the child's care, and are frequently inadequately informed about their child's condition and about what is being done and why. This can lead to frustration and anger which is often directed at the medical staff. If maximum co-operation between medical staff and parents is to be achieved, again an alternative to the acute care hospital must be found.

As well as extracting a large social and emotional toll on both the patient and the family, the acute care setting extracts a large toll in economic terms. There are dramatic reductions in the cost of home care compared with hospital care for respirator dependent patients.[10] The major saving is in the cost of nursing and medical staffing. Initial savings can be as high as 70% following transfer of respirator dependent patients to the home.[5]

Humanistic and economic rationales can be made for developing a home care program for respirator depend-

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ent quadraplegic patients. While it may be argued that the potential for rehabilitation in these individuals is limited, no one would argue that a loving home environment is not preferable to a hospital environment for the medically stable patient.

Essentials of Home Care Program

Survivors of high cervical cord injuries cannot be treated and discharged without follow-up. Their rehabilitation is life-long and they will require continuous nursing and medical surveillance. Therefore, it is essential to have a well co-ordinated program providing continuity for medical treatment and record keeping. In addition, it is important to co-ordinate all the care providers including medical staff, nurses, social workers, rehabilitation therapists, parents and the community. This co-ordination could best be accomplished by establishing regional centres to facilitate the transfer of the patient home, organizing the medical and para-medical support network, and with patient follow-up.[7] A home care program should address a number of issues to include the needs of both the patient and the family.

Any home care program must provide:

i) Access to Emergency Medical Care: The respirator dependent quadraplegic can be medically labile. Infections are primary medical complications. Respiratory and urinary tract infections are particularly frequent. Transporting the patient to the hospital without advanced preparation is difficult due to the amount and bulk of life support equipment. Consequently, it may be necessary to have medical staff available for house call on a 24-hour basis. The house visitor must be equipped to deal with most of the complications he is likely to encounter. This may require establishment of a fleet of mobile home care units stocked with the equipment and medications likely to be needed. Following assessment of the patient at home, the visiting physician may decide that admission of the patient to the hospital is indicated. This will require availability of vehicles capable of transporting the patient and his supportive equipment. Transportation services could probably also be provided by the mobile home care units. A second option is that the house visitors be specially trained paramedics in constant communication with primary care physicians based at the regional centre, so that decisions to transfer the patient or institute treatment at home could be made in conjunction with medical experts. The patient must be close to around-the-clock emergency medical care. This may require relocating the family close to a regional centre and into built up areas with well paved and maintained roads. It is difficult to predict the number of hospital visits the respirator dependent patient will require; however, studies have suggested that this number is lower than may be expected.[9, 10] Similarily, the length of stay in the hospital per visit would be hard to predict, depending on the patient's condition and the confidence that the attending physician has in the home care program. In any event, the patient must have ready access to the hospital both for routine check-ups and for medical treatment. Here again, the importance of continuity of care must be stressed, in order to avoid the redundancy and uncertainty likely to occur if a respirator dependent quadraplegic was to present at a hospital emergency ward where staff were unfamiliar with his current and past medical history.

ii) Access to Emergency Support in Event of Equipment Failure: Equipment failure can be the most devastating complication the patient is likely to encounter, therefore a number of precautions must be taken. First, an emergency generator must be available in the event of power failures. This role could potentially be filled by a battery unit, but this is much less reliable. Second, a backup respirator must be available in the event of failure of the first. This would of course require training the family in the operation of the units. The family must also be well trained in what to do in case of emergencies, and must learn to recognize signs of equipment failure by monitoring both the machine and the patient. Any time that equipment failure has occurred, medical personnel must be consulted for assessment of the patient. Thirdly, mechanical technicians must be available both for routine maintenance of the equipment and for emergency repairs. Once again, this would require establishment of a fleet of properly equipped vehicles. Routine maintenance visits should probably be at least bi-monthly, and emergency maintenance must be available on a 24-hour basis.

iii) Education for the Family: The respirator dependent quadraplegic will require assistance with all aspects of personal functioning, with nursing and with activities of daily living. These demands are even more taxing for caregivers to provide to younger children. The responsibility for provision of these needs will be placed primarily on the family and this will require a good deal of education and practice. The patient will require help with getting up in the morning and with going to bed, with dressing and undressing, washing, feeding and with ambulation. The nursing requirements will include tracheal aspiration, changing tracheostomy tubes, using hoists, bed pans and respirator equipment, and monitoring the patient for signs of any change in medical condition. The patient will have to be helped with activities of daily living such as household duties and shopping and with any recreational activities or hobbies. Ideally, most of this assistance will be provided by a caring family member, who will require tremendous support and encouragement from medical and paramedical personnel. The process of educating the new care givers must begin in the hospital long before the patient's discharge is arranged, and must continue long after the patient is at home. Education should include a complete explanation of the patient's needs and capabilities, and of what is expected of the care giver. The family must be aware that education is an ongoing process and should be encouraged to learn more about the child's condition and to keep abreast of changes and developments in medical and nursing care as they become available. There should be an expert available at all times to give advice and answer questions as they arise, and a system for testing the care givers level of understanding and the quality of their care provision should exist.

iv) Support for the Family: The workload placed on

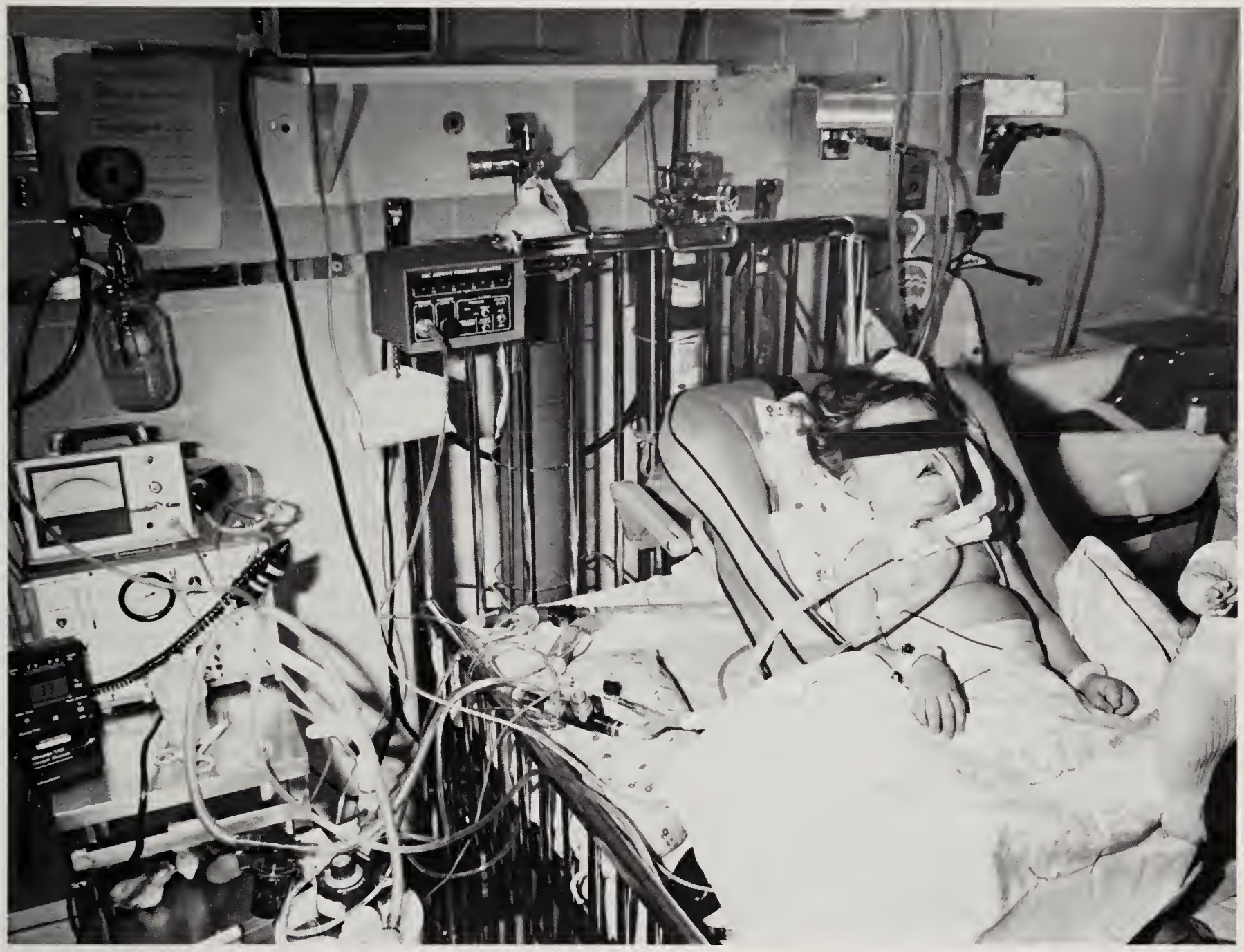

Figure 1. One year old female, permanent resident in Neonatal Intensive Care Unit, who is quadraplegic following birth trauma. She is ventilator dependent.

the family of the patient could be overwhelming, without proper support. Hence, if home care is to be successful, close attention must be paid to the needs of the family. Considerable support can come from the extended family, and additional support groups could include other parents within the program; visiting home makers to help with housework and nursing; weekend parents who could look after the child on occasional weekends, providing the parents with much needed rest and relaxation, and visiting nurses to monitor the patient's progress and discuss any problems the parents might be experiencing. In addition, there should be a hotline to help. Many of these services could be provided by volunteers, and resources of existing organizations, such as the United Way, could be tapped.

v) Rehabilitation: In the case of the high cervical quadraplegic, the amount of rehabilitation, i.e., functional improvement, that can be accomplished is limited. However, if the patient's full potential is to be achieved, a co-ordinated effort involving a team of therapists will be required. Many specialized devices such as the sip-and-puff wheelchair are becoming available, and the patient should be instructed in their use. Environmental controls are also being organized. The patient can be taught to communicate and a special tracheostomy tube allowing some air flow through the larynx may be extremely helpful. In the special case of children, provision must be made for continuing education, and vocational training. Wherever possible, the patient must be encouraged to take an interest and initiative in his own care.

vi) Home Re-modelling and Preparation: A home may require significant remodelling if it is to accommodate the patient. Structural modifications may include widening doorways and installing ramps or elevator devices at stairs. Temperature control is very important for high cervical quadraplegics since autonomic functioning is lost. Changes in temperature may require installation of special heating and cooling units. This in turn may affect ventilator requirements. Other technical and mechanical equipment which may be required or desirable include emergency generators, and technical aids such as sip-and-puff wheelchairs, computer terminals, page turners and other items as they become available.

vii) Co-ordination and Co-operation Between Medical Staff, Nurses, Social Workers, the Family and the Community: One of the most essential requirements for a successful home care program is co-ordination and co-operation of services. It ensures that all necessary

services are provided and that there is no unnecessary overlap or duplication. Wide discrepancies have been found throughout the United States between the level of service provided for different respirator dependent patients in home care programs, depending on who is responsible for their care.[4] Some patients have services duplicated while others are chronically underserviced. The principal reason for this is the lack of co-ordination between the various organizations involved, resulting in poorly defined jurisdictions and responsibilities. If these types of problems are to be avoided in Canada, we must learn from the experience of others and integrate the resources and talents of all services likely to be participants in a home care program into one well organized and co-ordinated mechanism.

Patient Selection Criteria

For the patient and his family to derive maximum benefit from being placed in a home care program, it is imperative that stringent criteria for selecting patients to be included in the program are developed. Criteria have been suggested by Goldberg et al.[5] Four categories have been outlined:

i) Medical Criteria: The patient's blood gases and metabolism should be physiologically stable. The child should be growing and developing appropriately. In addition, the patient should be free from complications requiring medical intervention for at least three months prior to discharge.

ii) Social-Environmental Criteria: The family must be willing and able to accept responsibility for care of the patient and they must fully understand what this implies. The home must have adequate space for the patient and his technical aids, and for care givers. The house must have adequate heating, lighting and electricity, and should be accessible to medical treatment in case of emergencies. An adequate social support network should be in place.

iii) Re-imbursement Criteria: It is important that the financial burden of patient care not be placed on the family. Goldberg[5] suggests that less than 100% reimbursement of the home care costs would present an economic disincentive and may result in an unsafe program. Funding could come from various levels of government, from hospitals involved in the program, from third party payment organizations such as life and disability insurance, and from charitable donations. A full accounting of the costs the family is likely to encounter should be made and financing should be organized prior to releasing the patient.

iv) Organizational Criteria: A well organized program capable of dealing with the needs of each individual patient must be in place prior to sending the patient home. This has been discussed at length in the previous section.

Re-introducing the Patient to the Home

A smooth transition from hospital to home care will require careful planning and co-ordination. A full assessment of the needs of both the patient and the family must be made prior to release. This assessment should include medical and nursing needs, financial needs, technical needs, housing needs, educational needs and social supportive needs. All of these must be accounted for and provided prior to release. Individuals involved in planning the discharge should include the primary care physician, the nurse, respirator therapists, social workers and rehabilitation therapists, home care program administrators, the family, and the patient himself.

It may be advisable to use a staged approach to reintroduce the patient to the home, with initial weekend visits followed by progressively longer stays until all involved feel comfortable and confident with the new arrangements. Careful monitoring of the patient and the family will be required initially to safeguard against unpredictable complications. As time goes by the intensity of monitoring and frequency of intervention can be decreased, but cannot be eliminated.

Conclusions

In recent years near epidemic numbers of people requiring long term life support measures are presenting for management which is largely due to the decreased mortality and morbidity associated with high cervical cord injuries. Many of these individuals currently spend prolonged periods of time in acute care hospitals, which is expensive in both human and economic terms. In this article, we have discussed an approach to the development of a home care program for those patients who qualify according to strict selection criteria. Both the patient and his family can derive social and spiritual benefit from being re-united in the home. With a well co-ordinated program and co-operation between medical and allied paramedical personnel, the transition from hospital to home care can be made smoothly and provide much satisfaction to all involved.

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Reflections on Aphrodisiacs

And Reuben went in the days of wheat harvest, and found mandrakes in the field, and brought them unto his mother, Leah ..... And Jacob came out of the field in the evening, and Leah went out to meet him, and said, "Thou must come in unto me, for surely I have hired thee with my son's mandrakes". And he lay with her that night."

Genesis. 30: 14-16.

HUMAN SEXUALITY

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John R. Keller, M.Litt B.Sc. 8T8

Abstract

Since the dawn of mankind, many drugs and chemicals have been used for their aphrodisiac properties. Street drugs, opiates, cocaine, marijuana, amyl nitrate, hallucinogens, alcohol, numerous plants and herbs have all been reported to increase sexual sensitivity and performance. To date, however, there is no scientific evidence to support the effectiveness of any substance as a predictable aphrodisiac. In the present review article, the aphrodisiac potential of cocaine, marijuana, alcohol, amyl nitrite and other recreational substances is discussed.

Introduction

Anecdotes about "love potions" which increase the user's sexual prowess and enjoyment have been found in the written records of our most ancient civilizations. Prior to 2000 BC, the Egyptians and Babylonians took substances to enhance their sexual prowess, and plants such as the mandrake are mentioned in the Old Testament. In ancient Greek mythology, Aphrodite, the goddess of love, emerged from the sea bringing erotic ecstasy to mankind. The cult of eternal love and sexuality which she initiated persists today in our search for aphrodisiacs, the use of which can intensify sexual desire, sensation and performance. With the ongoing sexual revolution, there has been a change in sexual values: a greater tolerance of premarital and extramarital sex, an increased emphasis on sexual gratification, a loosening of sexual inhibitions, a reduction in adherence to cherished traditions and taboos, and a more accepting atmosphere for sexual experimentation. The folklore is rich with tales of alchemists and magicians selling potions to those eager to become attractive to a desired lover or to increase their sexual prowess. The sexual effects of the ingested potions depended then, as today, more often on the gullibility of the individual and the prestige of the potion peddler than any true efficacy of the substances sold. In order to overcome sexual inadequacy, men and women have sought means to stimulate sexual excitement by resorting to food stuffs, plants, herbs, spices, alcohol, imagery, and even prayers to the gods[1]. By advertising sex stimulants with narratives of heightened and longer lasting sexual pleasure, many dealers receive millions of dollars from the public. When the product fails to live up to the expectation of the individual, the dissatisfied consumer rarely complains, because of unwanted publicity, but often goes on to buy a different "aphrodisiac" from another magazine.

Not only illicit drugs and alcohol but also numerous plants are believed to have sexually stimulating proper-

ties. In addition to increasing sexual sensation by ingesting chemicals, there are many other ways by which sexual arousal is known to take place (e.g., flagellation, voyeurism, pornography, etc), but in the present review only the aphrodisiac potential of the better known ingested agents will be described.

Exotic Aphrodisiacs

Donkey's milk, dried salamander, powdered rhinoceros horn, elephant's foot, salted crocodile, lion's penis, shark's fin, bee's wing, bat's blood, clams, ginseng, sheep gonads, mandrake and many other unusual substances have been (and still are) used in various cultures as aphrodisiacs.[2] However, all evidence regarding the aphrodisiac potential of these substances is based on folklore and subjective reports, and since no scientific appraisal of any of the above substances has been undertaken, all claims of their ability to modulate sexual pleasure remain unproven.

Alcohol

The ability of alcohol to reduce sexual inhibitions is legendary: as Ogden Nash has said, "Candy is dandy, but liquor is quicker". Regarding the aphrodisiac value of alcohol, Shakespeare wrote (Macbeth, Act II, Scene 3), "it increaseth the desire, but reduceth the performance" and this statement still holds true today.

Basically, ethanol is a central nervous system depressant. Recent work indicates that the increase in sexual desire found with the ingestion of alcohol is mainly psychosomatic, resulting from the individual's expectation that alcohol will enhance his/her sexual interest. While small doses of alcohol are reputed to increase sexual drives, larger doses have been known to render the individual (especially the male) incapable of performing sexually. In women, the effects of alcohol are variable.[12,13,14] A few studies report a decrease in the woman's ability to respond sexually, as reflected by a lack of vaginal lubrication, but others report almost the opposite. However, most studies have found that alcohol makes the woman more compliant and ready to initiate sex.

In men, alcohol excess is known to cause partial erections, impotence and delayed ejaculations. Masters and Johnson have noted that "Secondary impotence developing in the male in his late forties or early fifties has a higher incidence of direct association with excessive alcohol consumption than with any other single factor .... he frequently develops major concerns for sexual performance and rarely associates his initial disability with its direct cause".[15] However, in some instances alcohol is known to be beneficial in men with sexual problems. In men who have difficulty with premature ejaculation, drinking prior to having sex sometimes diminishes the central nervous system responses enough to delay ejaculation. Unfortunately, continued use of alcohol to bolster performance can lead to impotence and interference with a man's ability to maintain an erection. Today, however, alcohol serves less as an aphrodisiac and more as a powerful factor in social interactions, serving as a cue for sexual behavior — to attain responsivity to the social environment, courage, comfort and machismo in interpersonal exchanges.

Amyl Nitrite

This volatile inhalable nitrite is reputed to be the best aphrodisiac.[4,5] The basic pharmacological action of amyl nitrite is to relax vascular smooth muscle. As an aphrodisiac, amyl nitrite is known to dramatically increase sexual pleasure both during foreplay and during sexual intercourse. Surveys done among users of amyl nitrite to determine its aphrodisiac power reveal that most men and women experience a greatly potentiated sexual effect. Following inhalation of amyl nitrite, the user may experience a sudden feeling of warmth, exhilaration, and a sense of total freedom. During foreplay amyl nitrite has a disinhibitory effect, with some users claiming to experience a total body sensuality and sensitivity. During intercourse women users have reported that amyl nitrite facilitates penetration and that there is also "a feeling of being filled". It is believed that this enhanced perception of being filled and easier penetration is due to a combination of muscular relaxation of the vaginal wall and decreased pain perception. Because of numerous reports from both men and women that amyl nitrite facilitates anal intercourse (presumably due to relaxation of the anal sphincter), this agent is used by a number of homosexuals. Amyl nitrite has a true diversity, from its use for the treatment of angina pectoris via sublingual administration, to being inserted into the rectum (absorbed in the hemorrhoidal veins) for the purpose of enhancing the sensations of anal intercourse.

There are, however, a number of potential side effects which make the use of amyl nitrite as an aphrodisiac less than safe. Following inhalation, the most common side effects of amyl nitrite are headache and nausea. Furthermore, the toxicity of amyl nitrite following parenteral injection (especially intravenous) makes it a potentially lethal agent. Reports of fatal coronary artery occlusion and death from methemoglobinemia have been reported after the use of amyl nitrite.

Cantharides

Cantharides (Spanish fly) is an putative aphrodisiac which has enjoyed some popularity for a number of decades. Cantharides causes a pseudosexual excitement in the male by irritating the genitourinary tract. Long-term use is known to result in painful priapism (prolonged penile erection independent of sexual excitement) and increased vulnerability to urethral and bladder infections. Therefore, this substance is not recommended for use as an aphrodisiac.

Cocaine

The use of cocaine began with the natives of the Andes mountains of South America who chewed the leaf of the coca plant. Coca, from which cocaine is derived, is known as the "Divine Plant" of the Incas. For decades, coca, and its chief alkaloid, cocaine, have enjoyed reputations as powerful sexual stimulants. It was the Europeans who first documented the effects of cocaine on the natives of South America. They observed

that natives who ingested cocaine during various festivals developed a frenzied state of hypersexuality which was insatiable and undifferentiated. During this torrid sexual phase, which lasted up to several days, the natives were observed to have continued bouts of sexual coupling. At the end of the festival, the genitals of most men were swollen and mutilated. Despite the long history of cocaine use in South America, very little is known scientifically of the sexual effects of cocaine. Today, there is a powerful mythology surrounding enhanced sexual desire and performance among users of the drug.[6]

Cocaine is refined and is administered mainly by an intravenous injection or by inhalation. Since cocaine is known to effect the release of neurotransmitters in the brain, the claims of increased sexual interest may indeed have a physiological basis. Cocaine users express the belief that cocaine is a true aphrodisiac which causes intensified sexual experiences. Intravenous injections of cocaine have themselves been described as "heavenly and electrifying" orgasms, while inhalation of cocaine has been called a "charge of sexual energy". There is reportedly an immediate rush of euphoria, pleasure and ecstasy marked by hypersexuality. Within a few seconds to minutes, this rush is replaced by an extended period of excitation and arousal which may be followed by dysphoria, restlessness, hyperirritability, aggressiveness and, rarely, a paranoid psychosis. The aphrodisiac effect is lost at high doses because the adverse or distracting psychological effects of cocaine overwhelm the increase in sexual desire. In males it has been observed that physical exhaustion does set in after prolonged sexual activity. Most males complain that the sexual stimulation is non-specific. In order to relieve this excess sexual energy, some researchers have recommended that masturbation may help relieve the situation.[7,8]

Many recent studies indicate a high incidence of sexual dysfunction among chronic users of cocaine.[8] In males a high incidence of impotence has been found, and in both males and females anorgasmia has been reported. Despite this long term effect, the appeal of cocaine as an aphrodisiac continues. The reasons for cocaine's appeal can perhaps best be understood in terms of its association with power, wealth, charm and status. In addition, it is the one drug that almost always produces a sexually stimulating effect and is, therefore, thought of as the most reliable.

Marijuana

During the past 20-30 years, the use of marijuana as a social intoxicant has become much more commonplace. Throughout the recorded history of marijuana use, it has always been claimed that marijuana is a sexual stimulant or an aphrodisiac. However, marijuana is not always reliable in this regard and its aphrodisiac activity is dependent on the circumstances, time, surroundings, physical and psychological condition of the individual. The conclusion of many surveys and retrospective studies is that there is often an increased sexual awareness, satisfaction, feeling of emotional closeness, and pleasure when the substance is used. In general, women report an increase in sexual desire and men an increase in sexual enjoyment. The modulatory range in both sexes is very broad, with some reporting no particular change, and some even reporting an adverse effect upon sex. In some individuals marijuana produces a soporific effect, a condition not altogether ideal for sexual activity. There have been numerous studies on the actions of marijuana on users,[9,10,11] but one study in particular has indicated that there was an increased loss of virginity following use of marijuana.[11] In addition, the same study has shown that the mean age of the first experience of intercourse decreased, and conversely the mean frequency of copulation was increased among marijuana users.

Unlike cocaine, marijuana appears to have a more directed effect in some men and women, focusing sexual desire to an already familiar partner. This effect of promoting sexual fidelity is one which is rarely associated with the use of other substances. Numerous long-term studies indicate that with heavy marijuana use, loss of interest in sex frequently occurs over a period of time. In India, heavy doses of marijuana have been used to decrease hypersexuality in some patients. Studies in rats have shown that following chronic administration of marijuana, there were increasing lengths of time before both first mounting and ejaculation, increased post-ejaculatory interval lengths, and mountings of shorter duration.[11]

Despite the fact that many users of marijuana claim that this agent is an aphrodisiac, often only the most chronic users smoke marijuana for this purpose. For others, the use of marijuana is more likely secondary to their sexual and social behavior. Because of the availability, lesser expense compared to other illicit agents (like cocaine), and the ease of administration (smoking), marijuana is still one of the most popular agents used for its sexual effects.

Yohimbine

For many years yohimbine has been used as an aphrodisiac by some cultures. It is now known that the bark of the corynanthe yohimbine, contains this alkaloid. Yohimbine, which is an alpha sympathetic blocker, was previously incorporated into products containing methyltestosterone and nux vomica as a treatment for the male climacteric. These products, however, are no longer on the market. Recently, it has been shown that administration of yohimbine to males with erectile failure obtained improvement in some patients as long as the medication was continued.[3]

Other Recreational Drugs

Reports about the sexual effects of lysergic acid diethylamide (LSD) and other hallucinogens are largely subjective.[16,17,18] The effects of LSD and other hallucinogens upon sexual responses are mediated to a great extent by the conditions under which the drugs are taken, the setting, as well as the recipient's personality and psychological state. Some users report prolonged but less absorbing orgasms, others report diminished awareness of sexuality, and yet others report no effect. It is recommended that LSD be avoided completely. It

may increase the sex drive but is illegal, and this agent is completely unpredictable in its psychological actions.

Amphetamines are also said to heighten libido, improve sexual performance and reduce inhibitions when taken in large oral doses. Massive intravenous doses precipitate a rush, a visceral numbness and tingling resembling orgasm. Male users have been known to report an immediate positive effect of increased libido, prolonged erection and delayed ejaculation, and some women have been known to become sexually aggressive and dominant.

Narcotics like heroin and morphine can also affect sex drive. Heroin in the female has a enhancing effect of relaxation and disinhibition, although some women have reported dyspareunia (painful coitus) or vaginismus (painful spasm of the vagina). In males the primary aphrodisiac effect is related to delayed ejaculation and the ability to sustain an erection for longer periods. However, with chronic heroin use, males have reported failure to maintain an erection and also difficulties in ejaculation, and females have reported anorgasmia.

While many of these substances are claimed to act as sexual stimulants, there have, to date, been no controlled scientific experiments. Since personal expectation is such an important part of one's sexual experience, claims of aphrodisia must be refuted or repeated by objective controlled comparative studies in order to be of any value.

Conclusion

As long as humans place a high value on sexual attraction and performance, newer aphrodisiac preparations will continue to surface with the promise of enhancing sexual pleasure. However, if these agents are to serve any legitimate purpose, these chemicals will have to survive scientific scrutiny. Each will require careful evaluation of its effects on the user, its chemical content, its positive and negative side effects, plus its long term effects. Unfortunately, most of today's aphrodisiacs are usually impure or contaminated. Often this is the result of improper use of pesticides as in the cultivation of coca and marijuana plants, and severe toxicity may result upon ingestion.

In the 1980s, there are as yet no magical aphrodisiacs for increasing sexual pleasure. However, the perfume industry is attempting to isolate pheromones (substances secreted by animals to attract members of the opposite sex through the olfactory sense). It is believed by some that pheromones may truly be the only effective aphrodisiacs.[19] However the isolation of pheromones from the vaginal secretion of females and male sweat glands is still in its infancy and it remains to be seen before it ever becomes a reality. One wonders if the advent of the AIDS virus, and the decline of sexual promiscuity it seems to be causing, will lead to more of a reliance on psychologically oriented "aphrodisiacs" such as imagination and affection.

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In 20 years there could be no new drugs to imitate

Canada is the only western industrialized nation that allows prescription drugs to be copied before their patents expire.

Unless these regulations are changed the search for cures for arthritis, cancer, AIDS and other serious diseases will be compromised or eliminated altogether in Canada.

The rest of the problem is simple economics.

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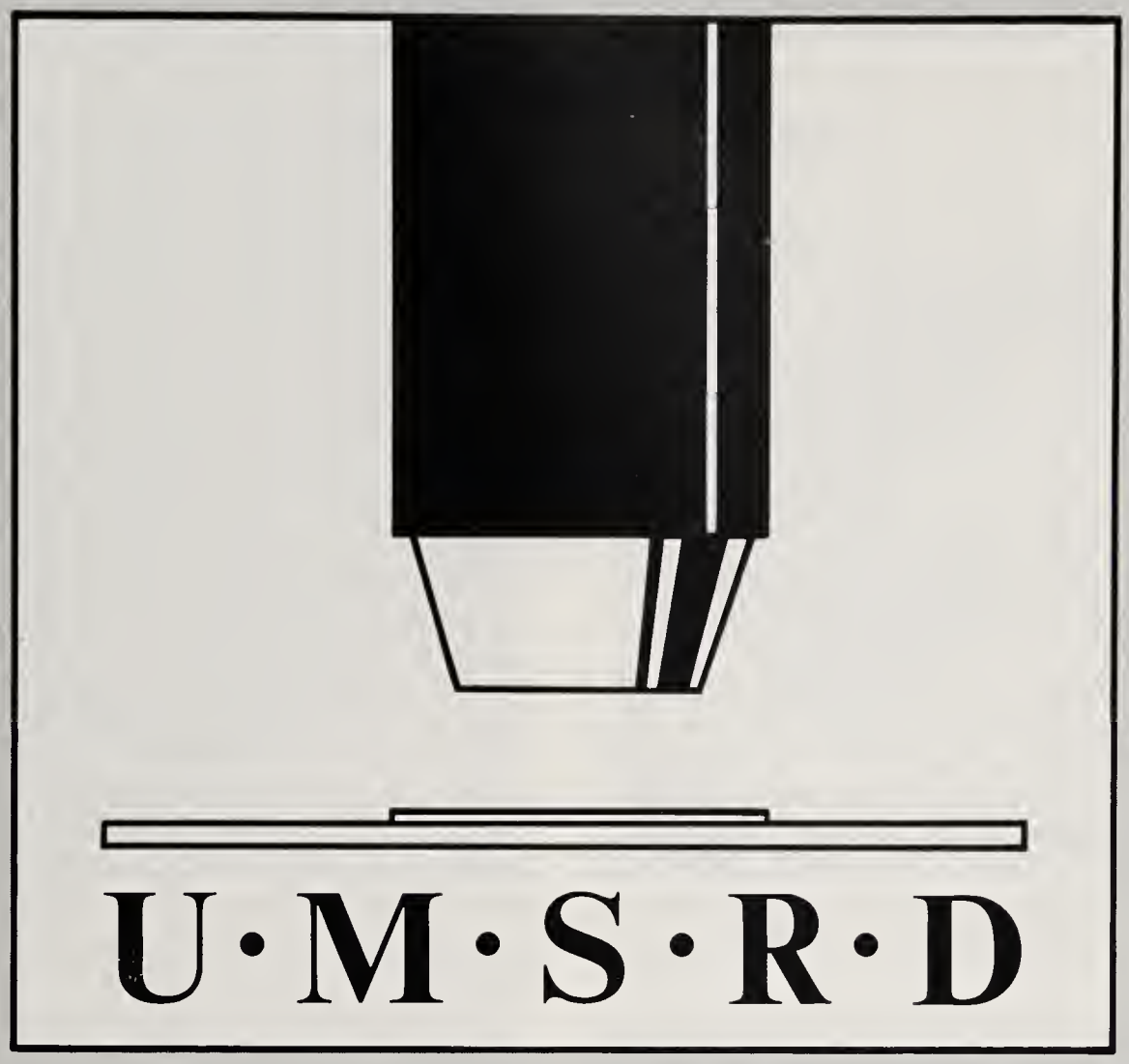

Undergraduate Medical Student Research Day

The second annual "Research Day" for undergraduate medical students will take place on December 1, 1987 in the Medical Sciences Building. All undergraduate students are eligible to submit abstracts for presentation. This year all abstracts meeting certain standards will be accepted. An ***elective credit*** *will be awarded to all students whose poster abstract is displayed. In addition, all participants will be invited to attend a special* ***Gala Dinner****. Finally,* ***prizes*** *will be offered for the best poster presentations. For more information please contact Dr. Niall Byrne — telephone number: 978-2051.*

Last year the following students were awarded the **George Brown Memorial Award for Research Accomplishment** for their presentations at the first annual **Undergraduate Medical Student Research Day** in 1986:

J. Chen; *The Growth Parameters of Native Indian Children in the Sioux Lookout Zone*
A. D'Urzo; *Airway Area by Acoustic Response Measurements and Computerized Tomography*
D. Feifel; *Centrally Administered Rat Hypothalamic Growth Hormone-Releasing Factor Differentially Affects Food Intake in Rats*
L. Harris; *Patterns of Ligand Binding to Normal, Regenerating, Preneoplastic and Neoplastic Rat Heptocytes*
Z. Miljkovic; *Voltage-Dependent Block of Excitating Amino Acid Currents by Pentobarbital*
J.M. Miyasaki; *On the Cause of Hyporeflexia in Holmes-Adie Syndrome*
M. Natarajan; *The Role of Plasma Membrane Phospholipids in Lipoprotein Binding to Human Adipocytes*
P. Pahapill; *Neuronal Experience Modifies Synaptic Post-Tetanic Potentiation*
S. Pallie; *Atherosclerotic Renovascular Hypertension: Comparison of Treatment Modalities*
B. Papsin; *The Growth Parameters of Native Indian Children in the Sioux Lookout Zone*
A. Sem; *Role of Sugars in T Cell Recognition*
J. Sheiner; *Food Intake Suppression by Histidine*

(Research Day logo by Jane Whitney, AAM)

Severe Hemoptysis

Folkert G. Zijlstra, M.D., Robert H. Hyland, M.D. F.R.C.P.(C), Donald P. Jones, M.D. F.R.C.S.(C), Eugene L. St. Louis, M.D. F.R.C.P.(C)

Severe Hemoptysis

A 17 year old male was admitted to hospital in November for investigation of hemoptysis lasting 2 months.

He was well until May 1986 when he developed an upper respiratory infection with a sore throat, low grade fever and a cough productive of scant yellow sputum but no blood. He was treated by his family doctor with a 2 week course of Ampicillin. His symptoms all cleared, and he was well until August 1986 when he had a similar episode, again treated with antibiotics. During the summer he worked in an auto shop doing body repairs.

In September 1986 for the first time he developed hemoptysis productive of approximately 1 cup of bright red blood every 2 days for 2 months. He had no other symptoms except for an episode of right-sided non-pleuritic chest pain for 2 weeks which improved spontaneously.

In November 1986 he sought medical attention when he noticed he was lightheaded on standing and was no longer able to run his usual 5 miles a day. His family doctor found his hemoglobin to be 71 g/L. At this point the patient was admitted for further investigation.

On examination he was a muscular young male in no distress. His blood pressure was 120/70 lying and 110/56 standing, his heart rate was 88/min and regular and his respiratory rate was 14/min. Ear, nose and throat examination was normal. Examination of the chest was normal and the only abnormal physical finding was a faint systolic ejection murmur at the left sternal border.

In hospital, investigations revealed a hemoglobin of 78 g/L (normal 135-180 g/L) with a mean corpuscular volume of 79 fl (normal 76-100 fl), serum iron 5 μmol/L (normal 11-27 μmol/L), total iron binding capacity 63 μmol/L (normal 42-72 μmol/L), saturation 0.08 (normal 0.20-0.50), ferritin 96 μg/L (normal 30-250 μg/L), reticulocyte count 167 x 10^9/L (normal 10-75 x 10^9/L), white blood cell count 7.6 x 10^9/L (normal 4.0-10.0 x 10^9/L and platelet count 374 x 10^9/L (normal 150-400 10^9/L). The coagulation studies revealed a normal prothrombin time and partial thromboplastin time and bleeding time. The serum creatinine was 87 μmol/L (normal 60-120 μmol/L), blood urea nitrogen 3.8 mmol/L (normal 3.0-7.0 mmol/L), 24 hour urine for protein 70 mg (normal 0.15 g/24 hrs) creatinine clearance 1.7 ml/sec. (normal 1.24-2.08 mL/S). Urine microscopy revealed no casts. Arterial blood gases on room air showed a pH of 7.44, a PCO_2 of 37 mm/Hg, and a PO_2 of 84 mmHg. Pulmonary function tests revealed normal flows and volumes with a hemoglobin corrected DLCO of 89% normal. His EKG was normal. His chest radiograph (Figure 1) was also normal, but the CT scan of the chest revealed a bilateral diffuse alveolar filling disease (Figure 2).

Other laboratory data revealed an ESR of 5 mm/hr (normal 0-20 mm/hr); a negative rheumatoid factor, antinuclear antibody and cryoglobulins and normal complement levels. Serum antibasement membrane antibodies were absent. Bronchoscopy was performed and revealed no endobronchial bleeding site. Bronchoalveolar lavage showed red fluid containing hemosiderin laden macrophages.

Figure 1(a)

Departments of Medicine, Surgery and Radiology, The Wellesley Hospital

Figure 1(a) and 1(b) Chest PA and lateral views. No cardiac, pulmonary vascular or lung parenchymal abnormaility is demonstrated.

With no evidence of extrapulmonary disease, infection, coagulopathy, or hemodynamic abnormality, the diagnosis of IPH was suspected. The diagnosis was confirmed on open lung biopsy which showed alveolar hemorrhage with no evidence of vasculitis or granulomas and negative immunofluorescence.

IPH is a rare disease occurring primarily in young people and characterized by recurrent episodes of hemoptysis, iron deficiency anemia, transient pulmonary infiltrates and no extrapulmonary involvement. Recurrent alveolar hemorrhage can lead to interstitial fibrosis, chronic dyspnea, clubbing and cor pulmonale.

The pathogenesis is unknown but reports have suggested an immune etiology based on 1) similarity to the alveolar hemorrhage of Goodpasture's syndrome and systemic lupus 2) response to immunosuppressive agents 3) high incidence (over 50% of cases) of an elevated serum IgA level.[2] There are reports that the electron microscopy shows focal rupture of the basement membrane but the significance of this is unknown.[6]

The prognosis is variable with spontaneous remissions occurring but the average duration of life is 2.5 years after the onset of symptoms.[7] Some patients die of massive alveolar hemorrhage while others have remissions for up to 20 years. Although success in treating acute episodes and sometimes inducing long term remissions has been reported in individual cases with steroids, azathioprine and plasmaphoresis, there have been no controlled studies.[8,9]

During our patient's admission he continued to have mild hemoptysis and was treated with plasmaphoresis. At the present time (one month after discharge) he is stable with minimal intermittent hemoptysis, a normal chest radiograph and a hemoglobin of 92 g/L. Consideration is being given to further therapy with steroids or immunosuppressive agents.

Figure 2(a) CT chest at a level just below the carina. Diffuse bilateral alveolar disease is revealed as poorly defined fluffy parenchymal infiltration. (see arrows).

Figure 2(b) CT chest of a *different patient*. Normal for comparison.

Answer

Hemoptysis is the expectoration of the blood from the lung. Epistaxis and hematemesis must be excluded. The bleeding can come from the tracheobronchial tree or from the pulmonary parenchyma. Broad categories of disease to be considered are: infections (bacterial, fungal, and parasitic), neoplasms, congenital disorders (A-V malformation), vascular diseases including vasculitis and recurrent pulmonary emboli with infarction, Goodpasture's syndrome, mitral stenosis and idiopathic pulmonary hemosiderosis.[1] Exacerbations of bronchitis and bronchiectasis are often accompanied by hemopty-

sis due to coughing induced trauma to enlarged superficial blood vessels in areas of chronic inflammation. The majority of these conditions can be excluded in this case by history alone. The physical examination, ENT examination and bronchoscopy were all normal and there was no laboratory evidence of a coagulopathy. The CT scan of the chest revealed a diffuse alveolar filling pattern which was not apparent on the plain chest radiograph. The differential diagnosis would include causes of diffuse alveolar hemorrhage: 1) Goodpasture's syndrome. 2) vasculitis. 3) idiopathic pulmonary hemosiderosis (IPH). The diagnosis of IPH is one of exclusion and requires ruling out the other causes listed above.[2]

Goodpasture's syndrome is mediated by antibasement membrane antibodies which bind specifically to antigens in the alveolus, glomerulus, renal tubule and choroid plexus. Alveolar hemorrhage in Goodpasture's syndrome is usually associated with glomerulonephritis and although our patient's renal function was normal with no proteinuria, hematuria or casts, the diagnosis could not be excluded because pulmonary hemorrhage may preceed the renal disease.[3] The absence of antibasement membrane antibodies in the blood goes against the diagnosis but basement membrane immunofluorescence is needed to absolutely exclude Goodpasture's syndrome.

Vasculitis can also cause diffuse alveolar hemorrhage. Systemic lupus can present with hemoptysis but there is usually evidence of systemic disease with extrapulmonary organ involvement and positive serologic markers. Lung biopsy specimens show deposits of complement and IgG in the alveolar walls and electron dense deposits in the capillary basement membrane.[4] Wegener's granulomatosis is characterized by necrotizing granulomas in the upper and lower airways with cavitating nodules on chest radiograph. During the summer, prior to the onset of hemoptysis, the patient worked in an autobody repair shop. At this time he worked with epoxy body fillers. There have been case reports of hemoptysis following inhalation of resin containing tri-mellitic anhydride. These patients however were all noted to be very ill with nausea, vomiting and fever.[5]

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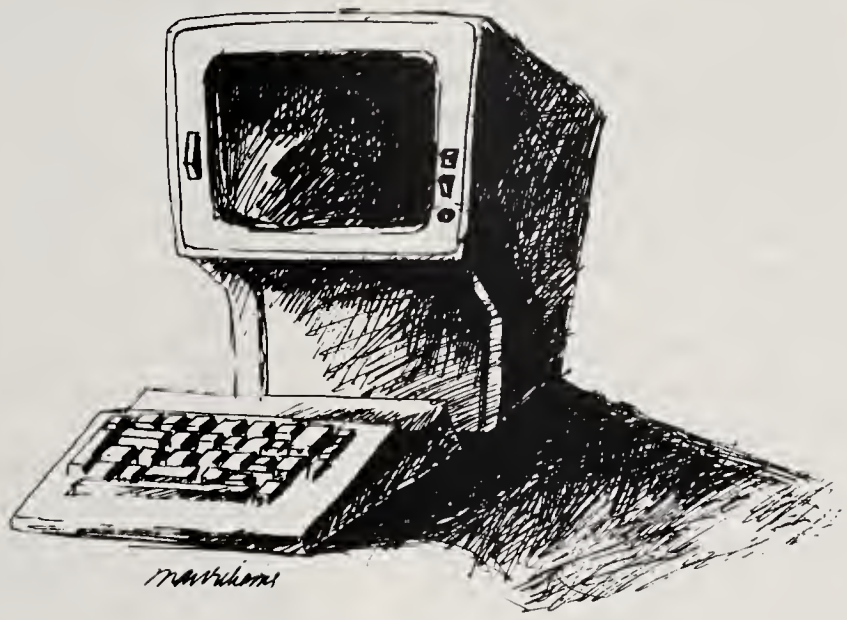

The National Board of Medical Examiners and Computerized Testing

Peter Wan, 8T8

The National Board of Medical Examiners (NBME), at its March 1985 Annual meeting, acted to approve proceeding with the implementation of computer-based testing (CBT)[1]. Plans call for the use of an interactive computer-based simulation model known as CBX, as well as computer delivered multiple choice questions (MCQs), first in 1989 in the National Board's Part III examination and, subsequently, in other examinations for licensure and certification in medicine[2].

History of CBX

As early as 1968, the NBME recognized that the then-emerging computer technology held great potential for enhancing the evaluation of professional competence. This vision became a reality as the result of the NBME's 15 year commitment to the continuing research and development essential for the evolution of the CBT program. Financial support over the years came from such prominent institutions as The Commonwealth Fund, the Carnegie Corporation of New York, the W.K. Kellogg Foundation, and the Health Resources and Services Administration of the US Department of Health and Human Services.

Current CBT Model

NBME's Part III examination has traditionally consisted of a MCQ component and a patient management problem (PMP) component. Both of these will be replaced by the CBT model.

The equipment necessary to allow NBME to successfully administer the test, ensure confidentiality of the test content, and provide a much faster medium on which to evaluate results consists of a central controlling computer with a data bank of questions and scenarios. Immediately before the time of the test, the encrypted data necessary to administer a test is sent onto the testing stations at various points on the continent. The individual test centers themselves are provided with computers (most likely microcomputers) that have software to decode the data and administer the test to the candidate.

MCQ Component

Since the computer-administered Part III will be given at many different testing sessions, multiple different (but equivalent) forms of the examination will be required. A special committee has created more than 600 new items to enhance the Part III test item pool of MCQs. Software for creating and administering MCQ examinations supported by interactive videodisc has been completed and appropriate orientation materials have been developed.

CBX Clinical Simulations

The computer-based simulation model is an unstructured, uncued simulation of medical practice in which the physician is presented with a clinical problem and is asked to make a diagnostic evaluation and institute management. Very few, if any, clues that were provided by the previous pen and paper format used in the PMPs will be provided here.

A record of every action taken by the physician dur-

ing the simulation is maintained by the computer. CBX is expected to provide a profile of physician performance that reflects clinical practice more closely than written PMPs; therefore, the introduction of CBX into examinations for medical licensure and certification should constitute a major step forward in evaluation, and contribute toward assuring the public of a candidate's capacity to provide safe and effective health care.

Simulations have been prepared by a case development committee and, to date, 162 have been set up. About 40 new cases will be added to the pool each year. After each simulation is developed, a separate scoring committee develops performance criteria for scoring case simulations. The criteria define and rank optimal actions that represent competent care in the management of the simulated patient. The scoring committee has developed criterion sets for 63 cases and continue to meet regularly to develop criteria for the remaining cases. Detailed scrutiny of the cases and the scoring keys is critical, since the presence of defects in the CBX cases at the time of examination administration could compromise the validity of scores.

Field Trials

Field trials comparing the tests and therapies ordered by physicians in their hospital practices with those ordered in CBX showed most of the orders and their timing were similar in the two settings. This simply suggested a physician will not change his/her method of diagnosis or treatment of a patient whether the patient is in hospital or simulated on a computer.

A second field trial was designed to evaluate aspects of the reliability and validity of CBX scores for measuring competence. Practitioners incurred significantly lower risk and cost scores than third year residents who in turn obtained significantly better scores than first year residents. First year residents did as well as third year residents in diagnostic logic and outcome scores.

Studies are underway to assess the effect of prior experience with computers on CBT performance and to test the effectiveness of the orientation program to familiarize examinees with a computer-based examination.

Future Developments

The NBME has established Computer-based Testing and Learning Corporation (CTL Corp.) in March 1986 in attempts to develop commercially available CBT systems for educational institutions, government agencies, state licensing boards, certifying boards, and any other entities concerned with education or with the qualification of those preparing for or engaging in occupations and professions licensed or otherwise regulated by governmental agencies to ensure the protection of the public health, safety, and welfare.

There will be greater flexibility in scheduling examinations. It will not be necessary for all those taking a given exam to be away from the institution on the same examination date, thus minimizing problems relating to patient coverage. There is the possibility of reporting scores more quickly to examinees than current schedules permit. CBX also has a promise for continuing medical education and the assessment of continuing competence.

Following the imminent success of the implementation of CBT to Part III of the NBME's Examination in 1989, Parts I and II will likely follow. One wonders when (not IF) the corresponding LMCC examinations in Canada will be computerized.

Acknowledgements

Many thanks to Donald E. Melnick M.D., Acting Vice President, Office of Institutional Development and Research, National Board of Medical Examiners, without whom this article could not have been written.

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1. The National Board Examiner, summer 1985; 32(3): 1-4.
2. The National Board Examiner, winter 1987; 34(1); 1-3.

Lessons in Basic Electrophysiology

Peter Lin 8T8

Author: James E. Randall
Department of Physiology, Indiana University,
Bloomington, IN 47405
Cost: N/A
Hardware: Apple II/II+/IIE
Disk Drive - 1

Subject: Electrophysiology - Membrane Potentials - CAI

Remember those ions and membrane potentials that you didn't really understand in electrophysiology? - well, here is a program that will clear it all up in three easy lessons (see figure 1). Each lesson separates out one important aspect and then explains it completely.

1) Lesson 1: Diffusion Forces on Ions: Ions move according to concentration gradients and so it is only logical that Lesson 1 deals with these forces of diffusion. This lesson, like the other two lessons, is plain and simple. On each screen there is a maximum of 5 lines of text and you can advance screens at your leisure. Even with my "tortoise-like" reading capabilities, I managed to complete each lesson in 10 to 15 minutes - so it doesn't take a tremendous amount of time. There is also a summary at the end of each lesson for us short

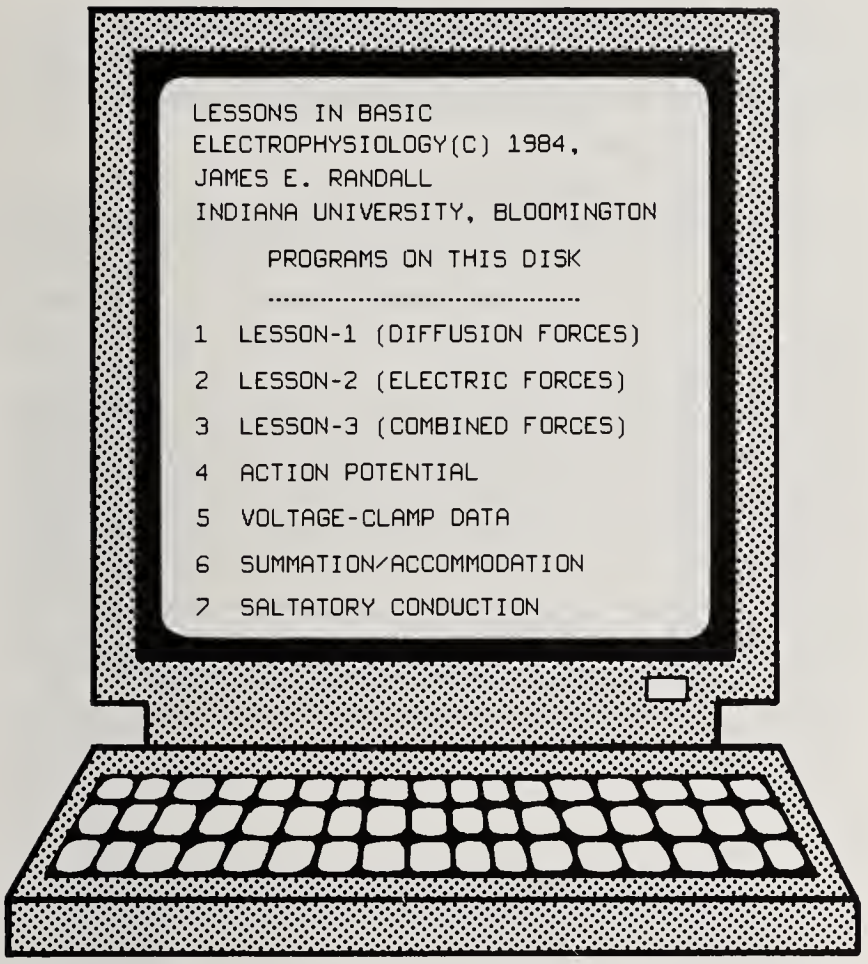

Figure 1

memory span people.

2) Lesson 2: Electric Forces on Ions: Since ions are charged, they therefore, succumb to electric forces as well as diffusion forces. Hence, lesson 2 is on the electric forces.

3) Lesson 3: Combined Diffusion and Electric Forces on Ions: This is the logical extension from lessons 1 and 2 and it is after this combined lesson that one realizes that electrophysiology is not that complicated.

The other options, in this package, are shown in figure 1. These are fun options and one could not possibly do them justice in such a short review. However, they must really take a back seat to the three lessons described above.

Comment:

The 3 lessons on electrophysiology are just ... just ... "awesome" (for lack of a better word). Electrophysiology, with respect to sodium, potassium and chloride, miraculously unfolds in an overwhelmingly logical manner before one's eyes. There are no "wild 7th dimensional visual effects" or anything "high tech" about these lessons. They are simply laid out in a concise, clear, and "Spock-like" manner. And at no point, did I experience that U of T phenomenon - "Fact over-load"!!

Overall, this package is very well worth-while for students and teachers alike. For those struggling with electrophysiology, get hold of this program. It won't teach you "Everything you wanted to know about electrophysiology but were afraid to ask" but it will clear up some basic concepts and maybe by understanding these concepts, the rest will fall magically into place.

To the author of the package, I'd like to extend my congratulations for a job well done and I hope he will continue to produce sequels of such high standards.

PRACPAC

Peter Lin 8T8

Author: R.D. Purves (1985)
Department of Pharmacology,
University of Otago, New Zealand
Cost: N/A
Hardware: Apple II/II+/IIE
Disk Drive - 1

Subject: Pharmacokinetics - CAI

Pracpac is really a mosaic of pharmacologic "tid-bits" as can be seen by the menu in figure 2. There are a total of six possible functions to choose from.

1) Simple Kinetics Animation: This basically demonstrates how drug concentrations change over time with different routes of drug administration. One selects the route (e.g. intravenous, intramuscular, oral and infusion) and the computer displays the resulting blood levels. Although these graphs can easily be found in any pharmacology textbook, this program brings in the dynamic dimension which enhances the impact of the curves. Hopefully, it will reinforce what has been learned from conventional teaching.

2) Drug Receptor Binding: This demonstrates how competitive antagonists function at the receptor site. You set the proportions of agonist versus antagonist and then watch how that affects the binding at the receptor site.

3) Organ-Bath Smooth Muscle: This is a simulation of smooth muscle responses to agonists and antagonists. Different dosages of agonist can be given and the results are displayed pictorially via a pulley system which indicates the amount of muscle contraction.

4) Acetylcholine and Blood Pressure: A continuous blood pressure tracing is used to demonstrate the effects of acetylcholine, atropine, and ganglion blockers on blood pressure and heart rate.

5) Catecholamines and Blood Pressure: Same as option (4) but one can administer adrenaline, noradrenaline, isoprenaline, alpha and beta blockers.

6) Anaesthesia Kinetics: This is similar to option (1) but it also displays lung concentrations as well as blood levels. There are two anaesthetics to choose from - nitrous oxide and methoxyflurane.

Comment:

PRACPAC is to pharmacology what Indiana Jones was to archaeology!!! Basically, this program is an attempt to demonstrate the dynamic nature of pharmacology and to bring it some life and action. Textbooks are great for factual information but are horrible for teaching dynamic processes, and hence pharmacokinetics can not be fully appreciated through this static medium. So there is definitely a place for this computer package in terms of teaching.

This program also indicates that computer simulations are feasible alternatives to doing live demonstrations. For example, options (4) and (5) can replace the

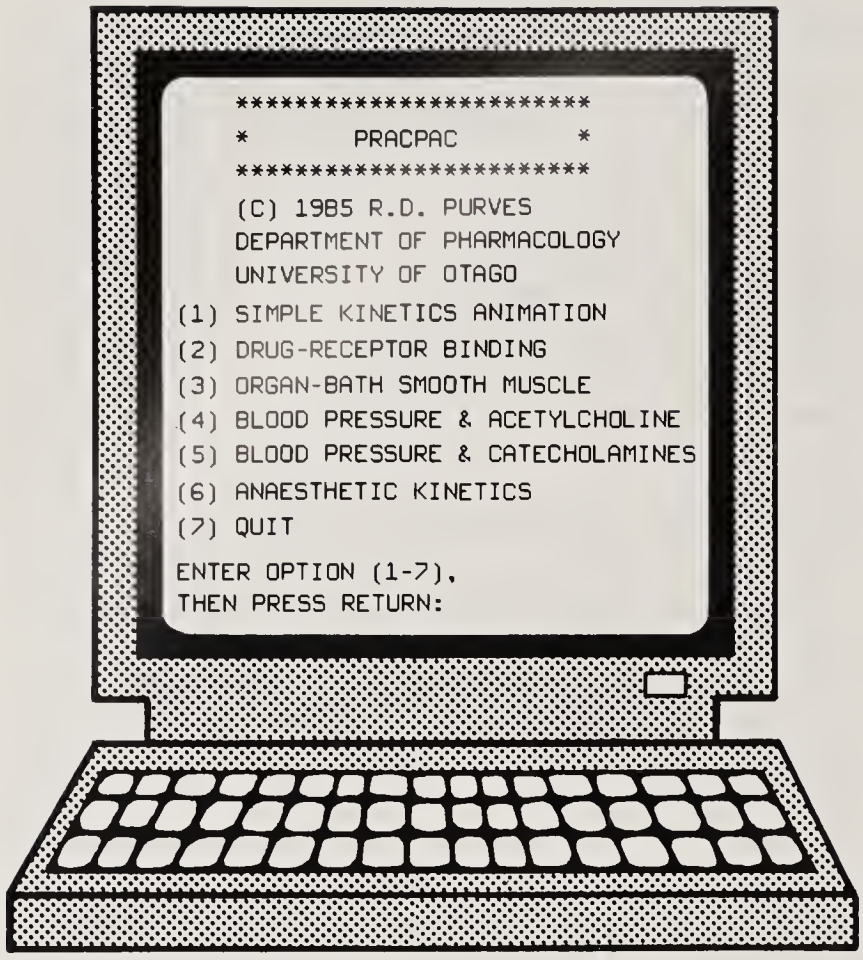

Figure 2

blood pressure experiments. I'm sure that students would not mind interacting with a computer in place of watching a live experiment for teaching purposes. This would simplify matters for both demonstrators and students.

The major problem with PRACPAC, at present, is a minor programming error. Once you are in one of the options, there is no way to get out except by resetting and re-running the main menu. This is a trivial mistake and can be easily corrected and I hope that the author will do so promptly.

Overall this is a good package for students. It presents the "same old information" in a new light which hopefully has a reinforcing effect.

SIMPAK

Peter Lin 8T8

Author: J.G. Blackman and R.D. Purves (1985)
Department of Pharmacology,
University of Otago, New Zealand
Cost: N/A
Hardware: APPLE II/II+/IIE
Disk Drive - 1

Subject: Pharmacokinetic Simulation - CAI

SIMPAK is a pharmacokinetic simulation package which deals with drug levels in the blood. The menu is shown in figure 3.

1) Named Drug Simulation: Out of a list of ten drugs, you can choose the drug and also specify the dosage. The program then plots out the blood levels over time. The drug can be repeated at the same dose or a different one at any time. The drug selection ranged from aspirin to turbocurarine and of course, ethanol made this top ten list.

2) Named Drug-Effect Simulation: This is like option (1) except that the effect of the drug is also plotted. The effect is represented as a percentage of the maximum effect. Here the drug list is much shorter - only three - digoxin, propranolol and turbocurarine. (Surprising that alcohol didn't make it!)

3) One Compartment Model: Recall in pharmacology the one compartment model? - well this is the computer version. Volume of distribution, dissociation parameters etc. can all be determined by you, the user, and according to these specifications, the computer will create your own unique drug. Having done so, you can then administer it via different routes and watch the rising blood levels.

4) Two Compartment Model: Similar to option (3)

5) Michaelis-Menton Model: Same set up as option (3)

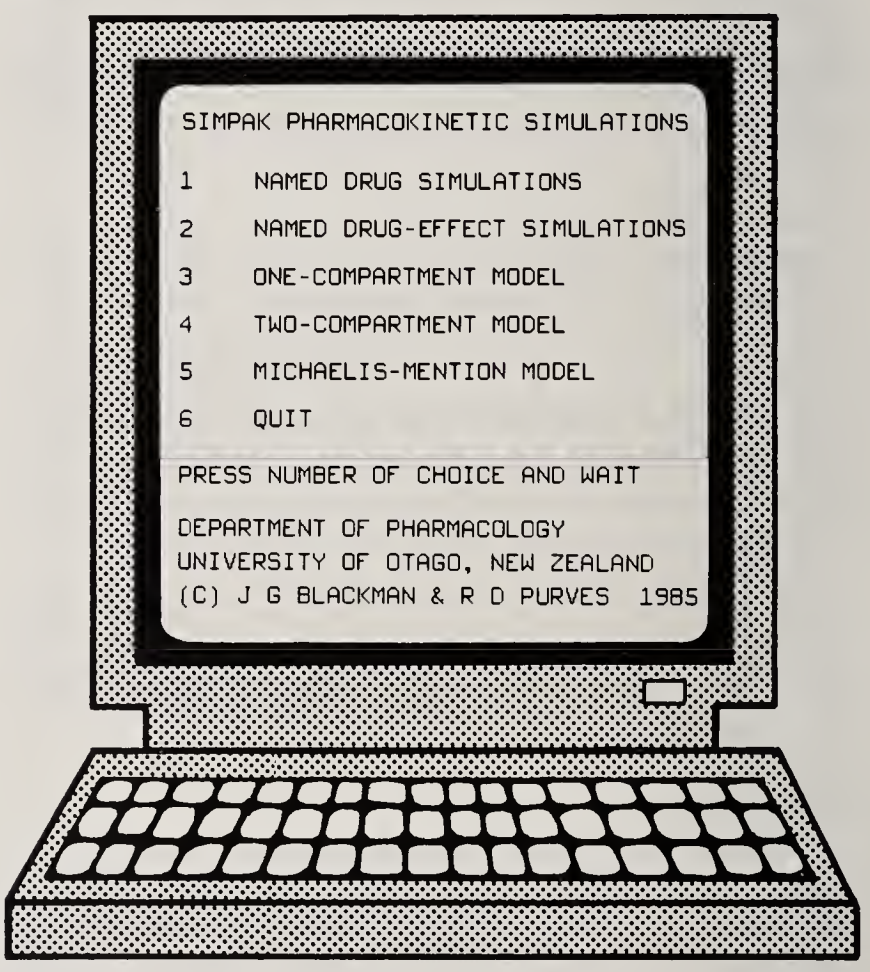
SIMPAK PHARMACOKINETIC SIMULATIONS
1 NAMED DRUG SIMULATIONS
2 NAMED DRUG-EFFECT SIMULATIONS
3 ONE-COMPARTMENT MODEL
4 TWO-COMPARTMENT MODEL
5 MICHAELIS-MENTION MODEL
6 QUIT
PRESS NUMBER OF CHOICE AND WAIT
DEPARTMENT OF PHARMACOLOGY
UNIVERSITY OF OTAGO, NEW ZEALAND
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Figure 3

Comment:

SIMPAK demonstrates one very important fact - "Drugs can accumulate" depending on when the doses are repeated, which drug is in question etc. etc.. Through all the options, one can see the drug accumulation clearly on the computer screen as the concentrations approached toxic levels. Hopefully, this visual image will remind us to think carefully each time we administer drugs - accumulations do occur (even at parties with a few quick drinks).

Options (3) to (5) are for the more inquisitive minds who want to fully understand how each drug parameter alters the drug kinetics. Definitely not for everybody but is very appropriate for those "keen" on pharmacokinetics.

NEWS UPDATES

Prevention of IDDM by Altering the Diet

Alfred Sem, 8T9

Toronto is a world renowned centre for diabetes research, thanks to the discovery of insulin by Drs. Banting and Best, as well as the continuation of high quality research in this field by the scientists here. Dr. J.M. Martin *et al.* at the Hospital for Sick Children recently observed that native Samoan children, without an adequate supply of cow milk, had a much lower incidence of insulin dependent diabetes melitus (IDDM) than children of Samoan immigrants in New Zealand, where there was plenty of cow milk readily available. Dr. Martin *et al.* investigated this phenomenon further by weaning BB rats with and without cow milk product (CMP) respectively. The group weaned with CMP had a higher incidence of IDDM than those weaned without CMP. On further investigation, it was found that at the onset of IDDM, those weaned with CMP had a higher titre of anti-β-lactoglobulin antibodies in the serum than those without CMP, β-lactoglobulin being a constituent in CMP, but not in human breast milk. Hence, it appears that presence of CMP in diet increases the incidence of diabetes, at least in BB rats. Can we then prevent diabetes by altering our diet? To answer this question, of course, more experimental work has to be done. Nevertheless, an excellent research strategy, directed at the prevention rather than at the cure of IDDM, has been formulated.

Duchenne Muscular Dystrophy Research Update

Malgorzata Nowaczyk, 8T9

Duchenne muscular dystrophy (DMD) is the most common of the muscular dystrophies: it affects one in 3000 male births. It is inherited in an X linked fashion; there are, however, females affected with this disease because of an X-autosome translocation and a selective inactivation of the normal X chromosome. The mild Becker muscular dystrophy (BMD) is an allelic variant of DMD. The most recent advances in the elucidation of the molecular defect in DMD and BMD come from the laboratory of Dr. Ronald G. Worton at the Department of Medical Genetics, Hospital for Sick Children, Toronto. The finding of genetic markers that segregate with the DMD mutation in Duchenne families was reported following research of a t(X;21) translocation female. This particular rearrangement placed the DMD gene from the X chromosome next to a long stretch of tandem repeats of genes for ribosomal RNA. Probes for ribosomal DNA allowed for the identification and cloning of a fragment of DNA spanning the translocation junction; subsequent chromosome walking resulted in the isolation of 250 kilobases of DNA surrounding the translocation junction. The two most recent reports (NATURE, July 30, 1987, and SCIENCE, September 25, 1987) demonstrate that the isolated DNA originated within the gene responsible for Duchenne and Becker muscular dystrophy. Several exons of the gene have been isolated and mapped. The gene is the largest to be isolated, and it covers about 2,000 kilobases of the X chromosome. This is also the first detailed characterisation of a constitutional translocation that results in a genetic disease. It is expected that knowledge of the DNA sequence will allow the generation of antibodies directed against synthetic peptides from the gene paving the way for isolation of the gene product and a complete understanding of the basic defect in these neuromuscular disorders.

Dr. John H. Dirks Appointed Dean of Medicine

Sumana Reddy, 8T9

Dr. John Dirks assumed the position of Dean of the Faculty of Medicine at the University of Toronto in July 1987. Dr. Dirks leaves the position of head of medicine at the University of British Columbia. He is currently director of the British Columbia Science Council, serves on the Research Committee of the Royal College of Physicians and Surgeons, the American Association of Physicians and the American Society for Clinical Investigation. Dr. Dirks has served on the editorial boards of several medical journals in Canada and the United States, and has held office in numerous national and international societies. In 1985 he received the medical award of the Kidney Foundation of Canada. He has published widely in the field of kidney research and has been an invited speaker at numerous conferences and medical symposia.

Myelin Associated Glycoprotein

John Attia, 8T9 & Sumana Reddy, 8T9

Dr. Rob Dunn of the Department of Medical Genetics and Dr. John Roder of the Mount Sinai Research Institute have recently cloned the gene for myelin associated glycoprotein (MAG) (Arquint *et al.*, PNAS 84: 600-604, 1987). MAG is one of a class of cell adhesion molecules. Excitement has been generated by this minor component of myelin protein (less than 1%), due to its possible role in signalling glial cells to start the process of myelination. It may therefore play a role in such diseases as multiple sclerosis. The myelination process has been recreated in vitro to study the effects of increased or decreased MAG expression. As well, biochemical characterization of MAG will be carried out and a search for the neuronal receptor for MAG has been launched.

BOOK REVIEWS

Exercises in Diagnostic Radiology - Chest, Abdomen, Bone and the Total Patient

by Lucy Frank Squire et al.
W.B. Saunders Company., Toronto, 1982. 118 pages. $53.95

Four separate volumes in the **Exercises in Diagnostic Radiology** series, authored by Lucy Frank Squire and several others, have been revised and combined into one book. This edition covers the major fields in radiology, leaving more specialized areas and advanced techniques to other volumes in the series. This book is meant as a companion to Squire's **Fundamentals of Radiology**, a well-known textbook. The aim of these exercises then, is not to teach the principles of radiology (which must be acquired elsewhere), but rather to provide an opportunity to apply these basics. The authors further state that they do not want to write a workbook, and they decry the "condescension" associated with such texts. While the authors have thus avoided the tendency to lead the reader step by step through every detail, the reader is expected to approach this text with a certain degree of sophistication.

The first three sections cover the chest, abdomen and bone while the fourth section is entitled the "total patient." The chest section (which opens the book) proceeds from a discussion of basic principles of radiography to examinations of chest x-rays. The bone section is well structured and didactic, while the abdomen section includes a brief outline of the systematic examination of an abdominal x-ray.

It is the "total patient" section that is most unique and intriguing. Here, short clinical histories are presented and the student is invited to deliberate on the appropriate courses of action. Case histories of patients are followed through several decision points that require some deft clinical skills. Consequently, this section is both useful and fun and it places x-rays in their proper context, illustrating where they are and are not indicated.

As this book is written by several authors, there is a noticeable difference of approach from section to section. Nevertheless, there is an appropriate range of difficulties among the exercises. As behooves a book on radiology, the pictures are well reproduced on glossy pages. There is also a useful index for each section, enabling the reader to examine the typical radiographic appearance of a particular condition.

In the companion textbook, Frank Squire states that she does not want to teach patterns of disease presentation radiographically, but rather to teach a suitable and reliable method of radiograph interpretation. There is a danger of using this book to learn the former - the responsibility is on the student to acquire the necessary basics before opening the book. Similarly, the radiographs in this book are presented along with short clinical histories and diagnoses are included in the answers. This is a boon for those attempting to integrate their clinical knowledge with their interest in radiology, but it also places further demands on the student, requiring him/her to have a firm grasp of the clinical conditions discussed.

Ultimately, radiographs are best learned through continued exposure and repetition. In this respect, this is a fine exercise book, but it is not a basic primer. Notwithstanding this fact, this book can help to break down the bewilderment that the medical student may initially feel upon approaching an x-ray. It will also serve as a handy accompaniment to students as their skills improve - a book that can help to increase the student's familiarity with radiology as he/she progresses in the acquisition of clinical skills.

Ahmed Bayoumi 8T9

Clinically Oriented Anatomy, 2nd Ed.

Keith L. Moore M.Sc., Ph.D., F.I.A.C., F.R.S.M.
Williams and Wilkins, Baltimore, 1985. 1101 pages. $55.25

Judging from Dr. Moore's previous works such as **The Developing Human, 3rd Ed.**, it comes as no surprise that this text is of equally high quality. Dr. Moore uses his years of experience in the subject to write a book that is very readable, accurate, and clear in its account of the anatomy of the human body. The text is neither core nor comprehensive, allowing the student to learn a bit more about a particular piece of anatomy, without having to read extensive amounts of material found in the thorough fashion of more comprehensive books.

The written text itself is augmented by an abundance of superb illustrations, especially those from **Grant's Atlas of Anatomy**. In discussing any particular aspect of anatomy, the author refers the reader to not one, but several illustrations, allowing the reader to understand the anatomy quickly and easily, especially in relation to other structures. Many additional illustrations explain anatomy that is often difficult and cumbersome to describe in words. In addition, Dr. Moore has included photographs illustrating surface anatomy. These teach the student the examination of a patient's internal anatomy without crossing the external boundary of the body. Tables have also been added, conveniently summarizing the attachments, main actions, and nerve supply of muscles. Thus the student need not spend

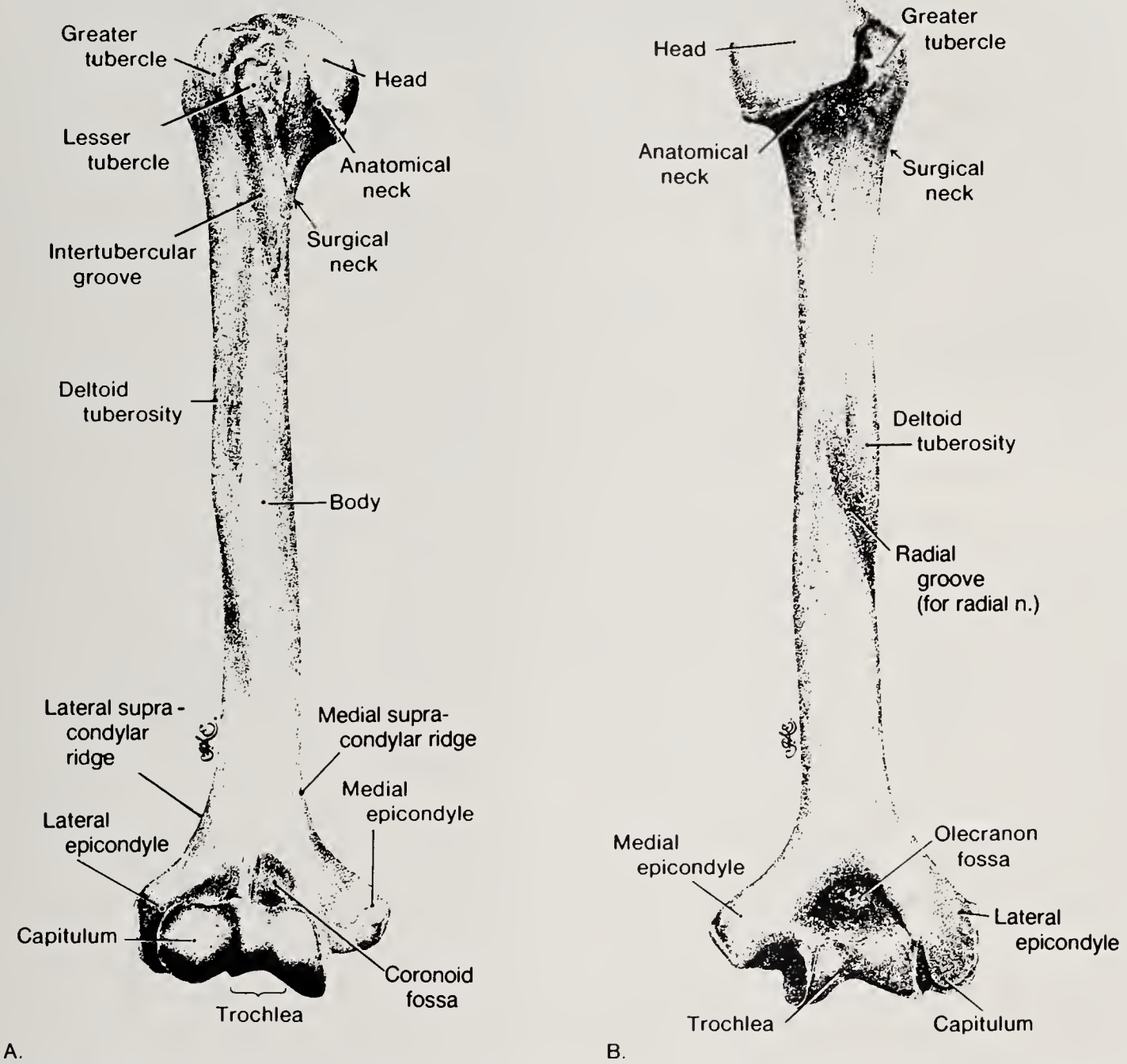

Figure 6-59. Drawings of the right humerus. *A*, anterior view. *B*, posterior view. Note the roughened area on the anterolateral surface of the body (shaft), called the deltoid tuberosity, into which the tendon of the deltoid muscle inserts (Figs. 6-49 and 6-62). Observe the radial groove which marks the course of the radial nerve and the profunda brachii artery (Fig. 6-69).

frustrating lengths of time searching the index for details of particular muscles.

The terminology that Dr. Moore uses also deserves mention. Anatomical terms used in the text are those prescribed by the internationally accepted **Nomina Anatomica** (5th Ed., Williams and Wilkins, 1983). However, it is true that language and jargon used most commonly in hospitals sometimes differs from that used in texts, whether for convenience or by tradition. Often, this may be a source of confusion between students and their clinicians. Therefore, in many instances, the author follows the anatomical term by the clinical term in parentheses, one example being, spiral organ (organ of Corti).

Perhaps the most significant feature of the text is that it allows the student to appreciate how a knowledge of anatomy can have genuine application. The text is virtually studded with sections isolated in blue that describe many common conditions found clinically. The sections describe these conditions along with their clinical findings and relate them directly to the anatomy discussed at hand. In addition, toward the end of each chapter, several clinical cases are presented and later discussed. These in particular can serve as quite a thirst-quencher, for most students crave for application of knowledge they obtain in lectures and textbooks. One only needs to browse through this text to realize that it is these two features that make "Clinically Oriented Anatomy" truly clinically oriented.

Murtaza Gulamhussein, 9T0

Useful Procedures in Medical Practice

P.W. Roberts, editor
Lea & Febiger, Philadelphia, 1986. 610 pages. $47.75

Stressed out at the prospect of being the only physician north of the tree line? Unsure of the bounds of your expertise as a primary care physician? Fret no longer, dear colleague. Our own Dr. P. Roberts, a family practitioner at Sunnybrook Medical Centre is here to help you with his text, **Useful Procedures in Medical Practice**. This recent publication is certain to become a standard for family doctors and clerks. It will also be of use for nurse practitioners performing the duties of physicians in underserviced areas.

Many of the procedures described are performed by specialists so that primary care physicians in urban centres should not attempt dentistry, Burr holes, etc. when such expertise is readily available. However, all of these procedures are explained in sufficient detail to allow even a clinical clerk to perform them. Thus, it serves to bridge the gaps that experience has not yet filled.

The writing is clear and concise with illustrations that clarify the text. Procedures are discussed with indications, precautions, equipment and method as subheadings. Subjects are covered from anesthesia to vascular access (a topic near and dear to every clerk) all written with consistently high quality. Try as I might, the only omissions of which I am aware deal with one of the physician's best friends, steroids. Since dexamethasone is mentioned as a Basic Eye medication, a section on diagnosis and treatment might be included. Along the same lines, the rheumatology section could include in its discussion of joint corticosteroid injection the maximum number of injections recommended in order to avoid abuse.

Dr. Roberts has succeeded in creating a comprehensive collaborative effort by members of our Faculty of Medicine. Its pithy nature will be a welcome relief to students inundated with circumstantial writing. **Useful Procedures in Medical Practice** definitely deserves a place in your imposing library.

Janis M. Miyasaki, 8T8

Mixed Blessings: Intensive Care for the Newborn

by Jeanne Harley Guillemin and Lynda Lytle Holmstrom
New York, Oxford University Press, 1986. 317 pages. $21 (U.S.)

"Would we be doing anything different in two or three months than we are doing today for this baby?" — this question is asked in various forms every day in neonatal intensive care units all over the country. It voices some of the major stresses of the field: rapid influx of new information, frequent exposure to death and dying, lack of personal contact with patients and families, and the need to make death and life decisions. In the midst of the latest technology harnessed to save the barely begun human lives one tends to forget what the struggle is all about. Two American sociologists make the human elements of the N.I.C.U. the subject of their revealing book: "Mixed Blessings".

The book analyses the organisation of the units and considers the viewpoint of both the professionals who work in the units and the institution of which the unit is a part. The authors describe the professional groupings, pecking order, handling of error, problem solving, decision making, policy generation and enforcement, and attitudes towards patients' and their families. Snatches of conversation, included as illustrations, give a taste of the emotionally charged atmosphere.

Analysis of the various medical professionals' attitude and approaches to neonatal intensive care consitute the major part of the book. N.I.C.U. physicians, nurses, and social workers are discussed in three major sections. There follows a discussion of the patient's career: where he comes from, his progress in N.I.C.U., and the discussion of possible outcomes. A section on family deals with the attitudes of parents toward the intensive care, their hopes and fears, and their interaction with the N.I.C.U. workers. The attitudes of professionals toward the patient and his family are bluntly presented in the "awful case" report. This part of the book is quite revealing: the authors report even the most outrageous statements made.

Most of the research was done at a major tertiary care teaching hospital: the "Northern Pediatric". Other nurseries in North America, Brazil, and Western Europe were visited for two or three days each for purposes of comparison. Although these descriptions resemble more brief impressions of tourists, rather than thorough research, the authors successfully present the differences in delivery of neonatal intensive care in various medical systems.

Following the international comparisons the authors return to their goal: setting out policy proposals that will assure that the well-being of infants will have priority over the allure of organisational efficiency and medical progress. The authors are quite critical of the modern N.I.C.U. functioning; they find the nurseries overly technical, intimidating, and unresponsive to family members. Parents, as well as social workers, psychiatrists, even nurses, are often excluded from decisions concerning the type of care, its continuation, or termination. The aggressive treatment of very low weight infants and infants likely to have severe physical or mental handicap is an object of the most scathing criticism.

Overall the book presents a very real and emotional picture of the N.I.C.U. It provides an excellent nonphysicians' perspective of the development of high technology for premature infants and its aggressive application. The authors' recommendations, although quite controversial, are carefully considered. The book presents enough information to provide an excellent introduction to the workings of N.I.C.U., without being so technical that it could not be read by parents, social workers, and even interested medical students.

Malgorzata Nowaczyk, 8T9

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